Innovation, Sciences et Développement économique Canada
Office de la Propriété Intellectuelle du Canada

Innovation, Science and Economic Development Canada
Canadian Intellectual Property Office

CA 3128426 A1 2020/08/06

(21) 3 128 426

(12) DEMANDE DE BREVET CANADIEN
CANADIAN PATENT APPLICATION

(13) A1

(86) Date de dépôt PCT/PCT Filing Date: 2020/01/20
(87) Date publication PCT/PCT Publication Date: 2020/08/06
(85) Entrée phase nationale/National Entry: 2021/07/30
(86) N° demande PCT/PCT Application No.: CN 2020/073222
(87) N° publication PCT/PCT Publication No.: 2020/156323
(30) Priorités/Priorities: 2019/01/31 (CNPCT/CN2019/074217); 2019/07/04 (CNPCT/CN2019/094726)

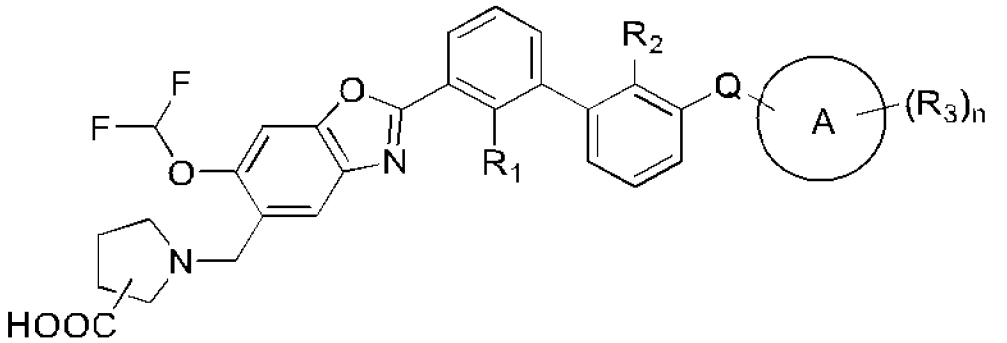
(51) Cl.Int./Int.Cl. *C07D 471/04* (2006.01), *A61K 31/423* (2006.01), *A61P 35/00* (2006.01), *A61P 37/00* (2006.01), *C07D 403/14* (2006.01), *C07D 413/14* (2006.01), *C07D 417/02* (2006.01)

(71) Demandeur/Applicant:
BETTA PHARMACEUTICALS CO., LTD., CN

(72) Inventeurs/Inventors:
WANG, YIQIAN, CN;
ZHANG, YAO, CN;
FU, BANG, CN;
WANG, JIABING, CN;
DING, LIEMING, CN

(74) Agent: NORTON ROSE FULBRIGHT CANADA LLP/S.E.N.C.R.L., S.R.L.

(54) Titre : IMMUNOMODULATEURS, COMPOSITIONS ET PROCEDES ASSOCIES
(54) Title: IMMUNOMODULATORS, COMPOSITIONS AND METHODS THEREOF



(I)

(57) Abrégé/Abstract:
Provided herein are compounds of Formula (I), methods of using the compounds as immunomodulators, and pharmaceutical compositions comprising such compounds. The compounds are useful in treating, preventing or ameliorating diseases or disorders such as cancer or infections.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
06 August 2020 (06.08.2020)

WIPO | PCT

(10) International Publication Number
WO 2020/156323 A1

(51) International Patent Classification:
C07D 471/04 (2006.01) *A61K 31/423* (2006.01)
C07D 417/02 (2006.01) *A61P 37/00* (2006.01)
C07D 413/14 (2006.01) *A61P 35/00* (2006.01)
C07D 403/14 (2006.01)

(21) International Application Number:
PCT/CN2020/073222

(22) International Filing Date:
20 January 2020 (20.01.2020)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
PCT/CN2019/074217
31 January 2019 (31.01.2019) CN
PCT/CN2019/094726
04 July 2019 (04.07.2019) CN

(71) Applicant: **BETTA PHARMACEUTICALS CO., LTD** [CN/CN]; 355 Xingzhong Rd., Yuhang, Hangzhou, Zhejiang 311100 (CN).

(72) Inventors: **WANG, Yiqian**; Building 29, Zone B, 1 North Disheng Rd., Business Development Area, Daxing, Beijing 100176 (CN). **ZHANG, Yao**; Building 29, Zone B, 1 North Disheng Rd., Business Development Area, Daxing, Beijing 100176 (CN). **FU, Bang**; Building 29, Zone B, 1 North Disheng Rd., Business Development Area, Daxing, Beijing 100176 (CN). **WANG, Jiabing**; Building 29, Zone B, 1 North Disheng Rd., Business Development Area, Daxing, Beijing 100176 (CN). **DING, Lieming**; 355 Xingzhong Rd., Yuhang, Hangzhou, Zhejiang 311100 (CN).

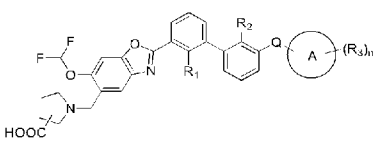
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report (Art. 21(3))*

WO 2020/156323 A1

(54) Title: IMMUNOMODULATORS, COMPOSITIONS AND METHODS THEREOF



(I)

(57) Abstract: Provided herein are compounds of Formula (I), methods of using the compounds as immunomodulators, and pharmaceutical compositions comprising such compounds. The compounds are useful in treating, preventing or ameliorating diseases or disorders such as cancer or infections.

IMMUNOMODULATORS, COMPOSITIONS AND METHODS THEREOF

FIELD OF THE INVENTION

The present invention relates to compounds that are inhibitors of PD-1/PD-L1 protein/protein interaction. The present invention also relates to pharmaceutical compositions comprising such compounds and methods of using such compounds in the treatment of cancer, pre-cancerous syndromes and other diseases associated with inhibition of PD-1/PD-L1 protein/protein interaction.

BACKGROUND OF THE INVENTION

Cancer immunotherapy has been increasingly utilized to treat advanced malignancies. The signaling network of immune checkpoints has attracted considerable attention. Several cancers are highly refractory to conventional chemotherapy. The survival of tumors in several cases is assisted by checkpoint immunomodulation to maintain the imbalance between immune surveillance and cancer cell proliferation. Immune checkpoint inhibitors are revolutionizing the treatment options and expectations for patients with cancer.

Programmed cell death-1 (PD-1), also known as CD279, is a cell surface receptor expressed on activated T cells, natural killer T cells, B cells, and macrophages. It functions as an intrinsic negative feedback system to prevent the activation of T-cells, which in turn reduces autoimmunity and promotes self-tolerance. In addition, PD- 1 is also known to play a critical role in the suppression of antigen-specific T cell response in diseases like cancer and viral infection. The interaction between PD-1 and PD-L1 results in a decrease in tumor infiltrating lymphocytes, a decrease in T-cell receptor mediated proliferation, and immune evasion by the cancerous cells. Immune suppression can be reversed by inhibiting the local interaction of PD-1 with PD- L1, and the effect is additive when the interaction of PD-1 with PD-L2 is blocked as well.

The development of a therapeutic approach to block the PD-1 mediated inhibitory signaling cascade in order to augment or "rescue" T cell response. Most of the currently approved medicines in immunotherapy are monoclonal antibodies. These monoclonal antibodies have shown impressive clinical results in treatment of several types of tumors. Therapeutic antibodies however exhibit several disadvantages such as limited tissue and tumor penetration,

very long half life time, lacking oral bioavailability, immunogenicity, and difficult and expensive production.

Recently, small molecules have been described to binding to PD-L1 in WO2015033299, WO2015033301, WO2015034820, WO2018183171, WO2018119224, WO2018119266, etc. Moreover, small molecule inhibitors that directly target PD-1 or PD-L1 are still not approved.

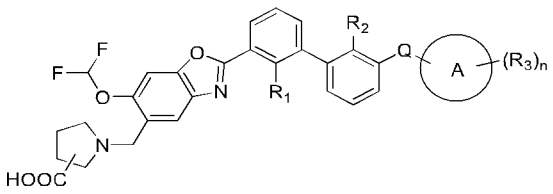
Accordingly, there is still great demand for more potent, and more easily administered therapeutics against PD-1/PD-L1 protein/protein interactions. In this invention, applicant discovered potent small molecules that can have activity as inhibitors of the interaction of PD-L1 with PD-1, and thus may be useful for therapeutic administration to enhance immunity against cancer and/or infectious diseases. These small molecules are expected to be useful as pharmaceuticals with desirable stability, solubility, bioavailability, therapeutic index and toxicity values that are crucial to become efficient medicines to promote human health.

Summary of Invention

The present invention relates to compounds that are used as inhibitors of the functional interaction between PD-L1 and PD-1. Inhibitors of the interaction between PD-L1 and PD-1 are useful in the treatment of cancers and infectious diseases.

The compounds of the invention have the general structures as Formula (I).

A compound of Formula (I), or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof,



Formula (I)

wherein,

R_1 and R_2 are each independently selected from halogen, CN, C_{1-6} alkyl, or C_{1-4} haloalkyl;

Q is a bond, -NH-, or $-(CH_2)_m-O-$;

Ring A is C_{5-6} aryl , C_{5-6} heteroaryl, C_{4-6} cycloalkyl or C_{4-6} heterocycloalkyl, wherein the C_{5-6} heteroaryl and C_{4-6} heterocycloalkyl optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O; or

Ring A is C_{8-10} fused bicyclic ring;

R_3 is H, halogen, $-(CH_2)_s-NR_4R_5$, C_{1-4} alkyl, C_{1-4} alkoxyl, hydroxyl, oxo, CN, $(CH_2)_q-CONR_4R_5$, $-COR_4$, $-NR_4R_5$, $-NR_4C(=O)NR_4R_5$, $-NR_4C(=NR_4)NR_4R_5$, $-S(O)_2R_4$, $-S(O)_2NR_4R_5$, $-S(O)R_4$, $-S(O)NR_4R_5$, C_{2-6} alkenyl, C_{2-6} alknyl , C_{1-6} haloalkyl, C_{5-6} aryl, C_{5-6} heteroaryl, C_{3-6}

cycloalkyl or C_{3-6} heterocycloalkyl, wherein the C_{5-6} heteroaryl and C_{3-6} heterocycloalkyl optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O; the C_{1-4} alkyl, C_{1-4} alkoxyl, C_{2-6} alkenyl, C_{2-6} alknyl, C_{1-6} haloalkyl, C_{5-6} aryl , C_{5-6} heteroaryl, C_{3-6} cycloalkyl and C_{3-6} heterocycloalkyl optionally substituted with one or more substitutents independently selected R_6 substituents;

R_4 and R_5 are each independently selected from H, C_{1-4} alkyl, or C_{3-6} cycloalkyl, C_{3-6} heterocyclyl, the C_{1-4} alkyl, C_{3-6} cycloalkyl, or C_{3-6} heterocyclyl optionally substituted with one or more substitutents independently selected R_6 substituents; or

R_4 and R_5 together with the atoms to which they are attached form a 4-10-member heterocyclic ring optionally substituted with one or more substituents independently selected R_6 substituents;

R_6 is H, halogen, hydroxyl, oxo, CN, $-(CH_2)_k-NR_7R_8$, $-COR_7$, $-NR_7R_8$, $-NR_7C(=O)NR_7R_8$, $-NR_7C(=NR_7)NR_7R_8$, $-S(O)_2R_7$, $-S(O)_2NR_7R_8$, $-S(O)R_7$, $-S(O)NR_7R_8$, or R_6 is selected from substituted or unsubstituted C_{1-4} alkyl, C_{1-4} alkoxyl, C_{2-6} alkenyl, C_{2-6} alknyl, C_{1-6} haloalkyl, C_{5-6} aryl , C_{5-6} heteroaryl, C_{3-10} heterocyclic ring, wherein the C_{5-6} heteroaryl and C_{3-10} heterocyclic ring optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O;

R_7 and R_8 are each independently selected from H, halogen, hydroxyl, oxo, CN, $-S(O)_2-$ C_{1-4} alkyl, $-NH_2$, -NH- C_{1-4} alkyl, $-(CH_2)-N(C_{1-4}$ alkyl$)_2$, or R_7 and R_8 are each independently selected from substituted or unsubstituted C_{1-4} alkyl, C_{1-4} alkoxyl, C_{2-6} alkenyl, C_{2-6} alknyl , C_{1-6} haloalkyl, C_{5-6} aryl , C_{5-6} heteroaryl, C_{3-6} cycloalkyl, C_{3-6} heterocycloalkyl; wherein the C_{5-6} heteroaryl and C_{3-6} heterocycloalkyl optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O;

m, n, q, k and s are each independently selected from 0, 1, 2, 3 or 4.

In some embodiments of Formula (I), wherein, R_3 is H, halogen, $-(CH_2)_s-NR_4R_5$, C_{1-4} alkyl, C_{1-4} alkoxyl, hydroxyl, oxo, CN, $(CH_2)_q-CONR_4R_5$, $-NR_4R_5$, $-NR_4C(=NR_4)NR_4R_5$, $-S(O)_2R_4$, C_{2-6} alkenyl, C_{2-6} alknyl, C_{1-6} haloalkyl or C_{3-6} heterocycloalkyl, wherein the C_{3-6} heterocycloalkyl optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O; the C_{1-4} alkyl, C_{1-4} alkoxyl, C_{2-6} alkenyl, C_{2-6} alknyl , C_{1-6} haloalkyl, and C_{3-6} heterocycloalkyl optionally substituted with one or more substitutents independently selected R_6 substituents.

In some embodiments of Formula (I), wherein, R_3 is H, halogen, $-(CH_2)_s-NR_4R_5$, -CN, $-S(O)_2R_4$, C_{1-4} alkyl, C_{1-4} alkoxyl, the $-(CH_2)_s-NR_4R_5$, C_{1-4} alkyl, C_{1-4} alkoxyl optionally substituted with one or more substitutents independently selected R_6 substituents.

In some embodiments of Formula (I), wherein, R_6 is H, halogen, hydroxyl, oxo, CN, $-(CH_2)_k-NR_7R_8$, $-COR_7$, $-NR_7R_8$, $-NR_7C(=O)NR_7R_8$, $-S(O)_2R_7$ or R_6 is selected from substituted

or unsubstituted C_{1-4} alkyl, C_{1-4} alkoxyl, C_{2-6} alkenyl, C_{2-6} alknyl, C_{1-6} haloalkyl, C_{5-6} aryl, C_{5-6} heteroaryl, C_{3-10} heterocyclic ring, wherein the C_{5-6} heteroaryl and C_{3-10} heterocyclic ring optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O.

In some embodiments of Formula (I), wherein, R_6 is H, halogen, hydroxyl, oxo, CN, -(CH_2)-N-$(C_{1-4}$ alkyl$)_2$, -(CH_2)-NH2, -N-$(C_{1-4}$ alkyl$)_2$,-NH_2, -CO-N-$(C_{1-4}$ alkyl$)_2$, -CO-NH_2,- $S(O)_2$-C_{1-4} alkyl, C_{1-4} alkyl-OH, C_{1-4} alkyl, C_{1-4} alkoxyl, C_{2-6} alkenyl, C_{2-6} alknyl, C_{1-6} haloalkyl, C_{5-6} aryl, C_{5-6} heteroaryl, C_{3-10} heterocyclic ring, wherein the C_{5-6} heteroaryl and C_{3-10} heterocyclic ring optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O.

In some embodiments of Formula (I), R_6 is halogen, oxo, -OH, $-NH_2$, $-N(CH_3)_2$, -C_{1-4} alkyl-OH, -C_{1-4} alkyl-NH-CH_3, -NH-C_{1-4} alkyl, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxyl, C_{5-6} aryl, C_{5-6} heteroaryl, C_{3-6} heterocyclyl, guanidine, or sulfone.

In some embodiments of Formula (I), wherein,

R_1 and R_2 are each independently selected from halogen, CN, -C_{1-6}alkyl, or -C_{1-4} haloalkyl;

Q is a bond, -NH-, or -$(CH_2)_m$-O-;

ring A is C_{5-6} aryl or C_{5-6} heteroaryl ring, wherein the C_{5-6} heteroaryl ring optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O; or

ring A is C_{8-10} fused bicyclic ring;

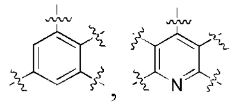
R_3 is H, halogen, -$(CH_2)_s$-NR_4R_5, -C_{1-4} alkyl, -C_{1-4} alkoxyl, the -$(CH_2)_s$-NR_4R_5, -C_{1-4} alkyl, -C_{1-4} alkoxyl optionally substituted with one or more substitutents independently selected from halogen, -C_{1-4} alkyl, -C_{1-4} haloalkyl, -C_{1-4} alkoxyl, C_{5-6} heteroaryl, C_{5-6} aryl, carboxyl, amino, hydroxyl, guanidine, or sulfone;

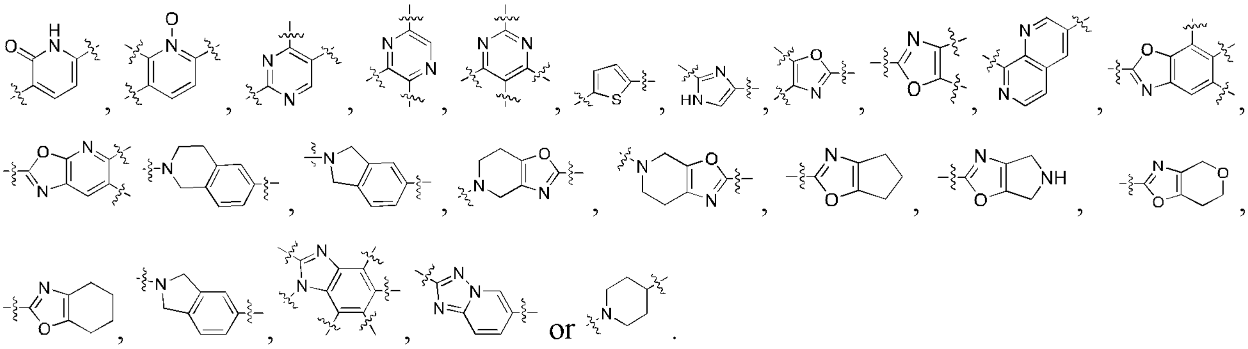
R_4 and R_5 are each independently selected from H, -C_{1-4} alkyl, or C_{3-6} cycloalkyl, C_{3-6} heterocyclyl, the -C_{1-4} alkyl, or C_{3-6} cycloalkyl, C_{3-6} heterocyclyl optionally substituted with halogen, -OH, $N(CH_3)_2$, -C_{1-4} alkyl, -C_{1-4} haloalkyl, -C_{3-6} heterocyclyl, -NH-C_{1-4} alkyl, or sulfone; or

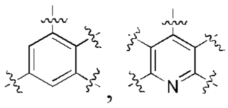
R_4 and R_5 together with the atoms to which they are attached form a 4- to 6-member heterocyclic ring optionally substituted with one or more substituents independently selected from -OH, $-N(CH_3)_2$, $-NH_2$, oxo, halogen, -C_{1-4} alkyl, -C_{1-4} alkoxyl, -C_{1-4} alkyl-OH, -C_{1-4} alkyl-NH-CH_3, or sulfone;

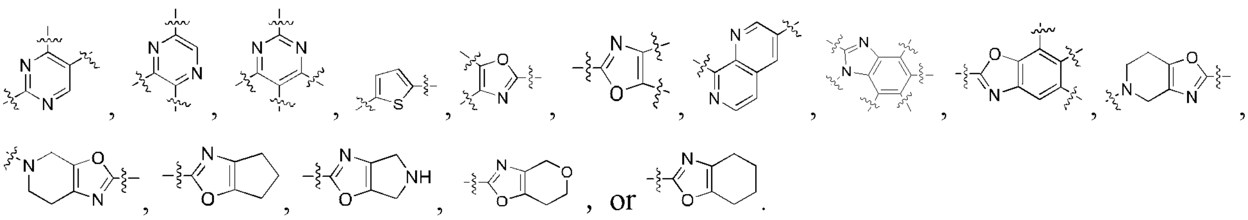
m, n and s are each independently selected from 0, 1, 2, 3 or 4.

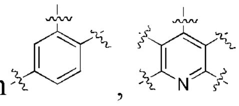
In some embodiments of Formula (I), wherein, wherein Q is selected from bond, -NH- or-CH_2-O-.

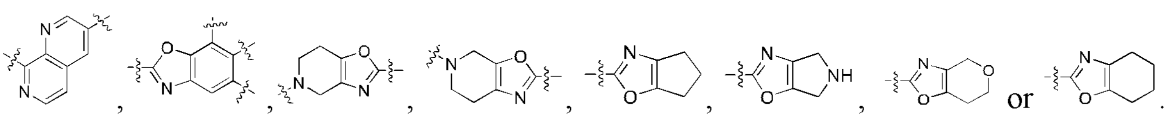
In some embodiments of Formula (I), wherein ring A is selected from 



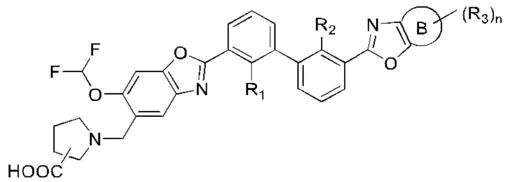
In some embodiments of Formula (I), wherein ring A is selected from 



In some embodiments of Formula (I), wherein ring A is selected from 



In some embodiments, the compound is of Formula (II):



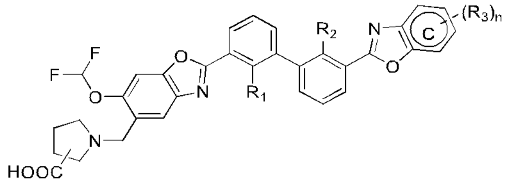
Formula (II)

or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein,

ring B is C_{5-6} cycloalkyl or C_{5-6} heterocycloalkyl;

R_1, R_2, R_3 and the subscript n are as defined in any embodiments of Formula (I).

In some embodiments, the compound is of Formula (III):



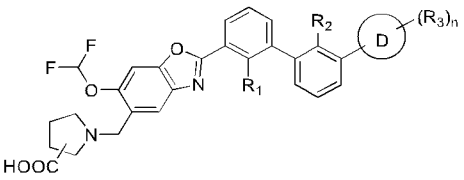
Formula (III)

or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein,

ring C is phenyl or heteroaryl, and the heteroaryl comprising 1, 2 or 3 N;

R_1, R_2, R_3 and the subscript n are as defined in any embodiments of Formula (I).

In some embodiments, the compound is of Formula (IV):



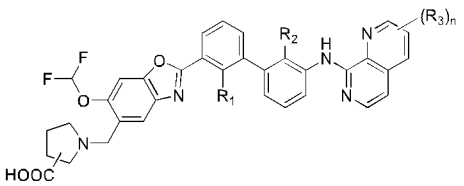
Formula (IV)

or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein,

ring D is C_{5-6} aryl, C_{5-6} heteroaryl, or C_{5-6} heterocycloalkyl, and the C_{5-6} heteroaryl and C_{5-6} heterocycloalkyl optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O;

R_1, R_2, R_3 and the subscript n are as defined in any embodiments of Formula (I).

In some embodiments, the compound is of Formula (V):

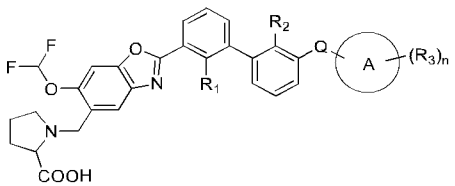


Formula (V)

or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein,

R_1, R_2, R_3 and the subscript n are as defined in any embodiments of Formula (I).

In some embodiments, the compound is of Formula (VI):



Formula (VI)

or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein,

ring A, Q, R_1, R_2, R_3 and the subscript n are as defined in any embodiments of Formula (I).

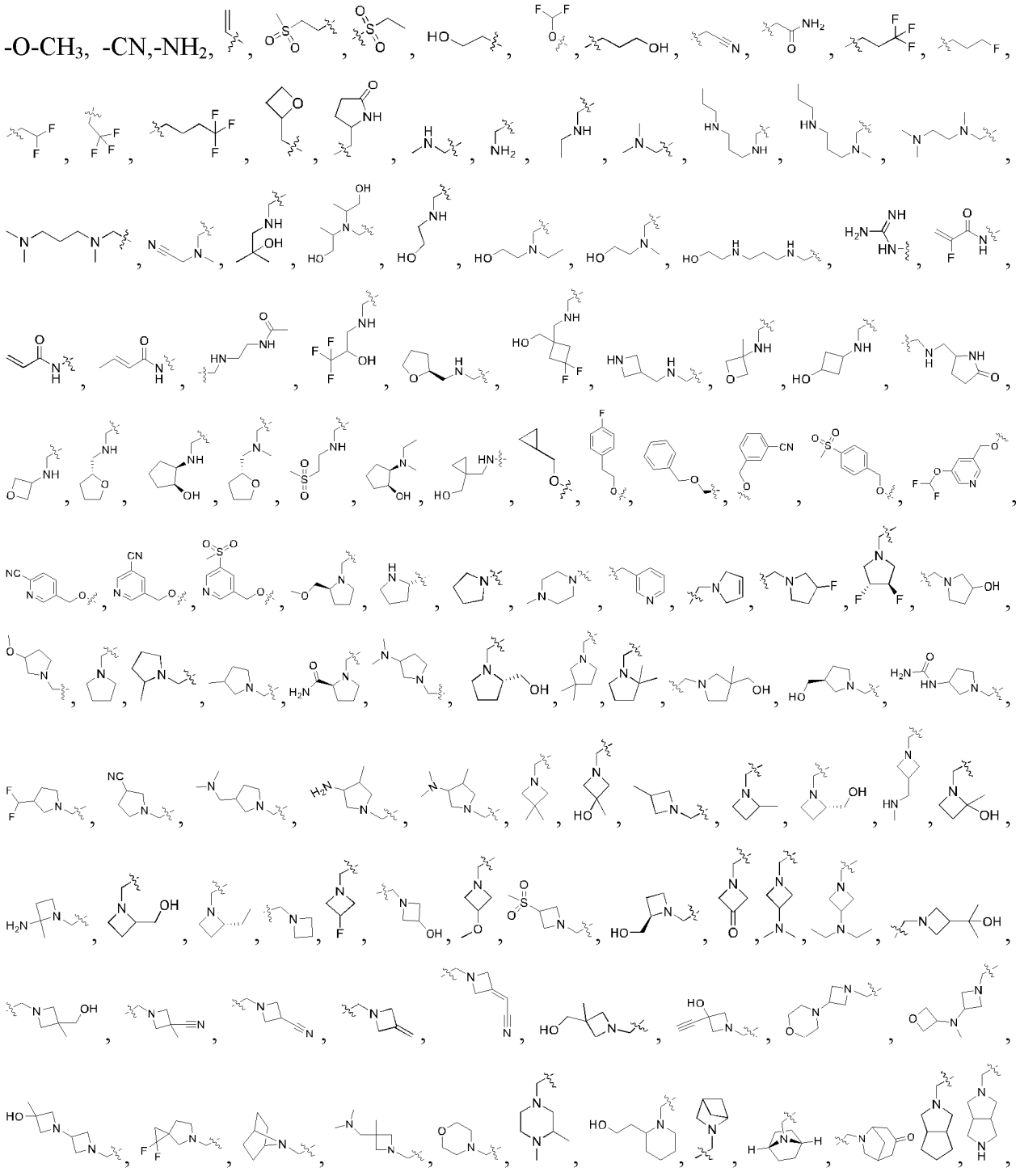
In some embodiments, wherein, R_1 is selected from selected from F, Cl, $-CH_3$, -CN or -O-

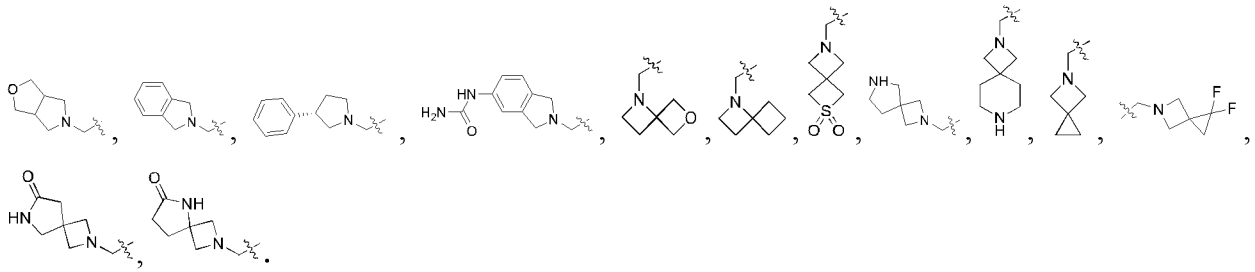
CH_3.

In some embodiments, wherein, R_1 is selected from selected from $-CH_3$, F, or $-O-CH_3$.

In some embodiments, wherein, R_2 is selected from $-CH_3$, F, Cl, or Br.

In some embodiments, wherein, R_2 is $-CH_3$.

In some embodiments, wherein, R_3 is selected from H, F, Cl, $-CH_3$, $-CF_3$, $-O-CF_3$, $-O-CHF_2$, $-O-CH_3$, $-CN$,$-NH_2$, 



In some embodiments, wherein n is 1, 2 or 3.

In some embodiments, wherein m is 1.

In some embodiments, wherein s is 1.

In some embodiments, wherein q is 1.

In some embodiments, wherein k is 1.

In some embodiments of Formula I, wherein the compound is:

1) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((((1R,2S)-2-hydroxycyclopentyl)(methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

2) (2'S)-(((2,2'-dimethyl-[1,1'-biphenyl]-3,3'-diyl)bis(6-(difluoromethoxy)benzo[d]oxazole-2,5-diyl))bis(methylene))di-L-proline;

3) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((S)-2-(methoxycarbonyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

4) ((2-(2'-cyano-3'-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

5) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

6) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2'-fluoro-2-methyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

7) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((2-hydroxyethyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

8) ((2-(3'-(5-(azetidin-1-ylmethyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

9) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-fluoroazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

10) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-fluoropyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

11) ((2-(3'-(5-(((S)-2-carbamoylpyrrolidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

12) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((S)-2-(hydroxymethyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

13) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(morpholinomethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

14) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-hydroxypyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

15) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((methylamino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

16) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((dimethylamino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

17) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((2-hydroxyethyl)(methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

18) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((3R,4R)-3,4-difluoropyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

19) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((((S)-5-oxopyrrolidin-2-yl)methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

20) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-hydroxyazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

21) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((ethylamino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

22) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((3,3,3-trifluoro-2-hydroxypropyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

23) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3,4-dimethylpiperazin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

24) ((2-(3'-(5-(aminomethyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

25) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((((1R,2S)-2-hydroxycyclopentyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

26) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((((1R,2S)-2-hydroxycyclopentyl)(methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-D-proline;

27) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((((1S,2R)-2-hydroxycyclopentyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

28) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((oxetan-3-ylamino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

29) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((((R)-tetrahydrofuran-2-yl)methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

30) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((methyl(((R)-tetrahydrofuran-2-yl)methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

31) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((S)-2-(hydroxymethyl)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

32) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((2-(methylsulfonyl)ethyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

33) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-(dimethylamino)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

34) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

35) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((R)-2-(hydroxymethyl)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

36) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((2-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

37) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((2-hydroxy-2-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

38) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((2-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

39) ((2-(3'-(5-((6-oxa-1-azaspiro[3.3]heptan-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

40) ((2-(3'-(5-((2-amino-2-methylazetidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

41) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-(methylsulfonyl)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

42) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((R)-2-ethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

43) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-methoxyazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

44) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-hydroxy-3-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

45) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-((methylamino)methyl)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

46) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-oxoazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

47) ((2-(3'-(5-((2-oxa-6-azaspiro[3.3]heptan-6-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

48) ((2-(3'-(5-((2-azaspiro[3.3]heptan-2-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

49) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((hexahydrocyclopenta[c]pyrrol-2(1H)-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

50) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

51) ((2-(3'-(5-((2,7-diazaspiro[3.5]nonan-2-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

52) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((3-(propylamino)propyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

53) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((methyl(3-(propylamino)propyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

54) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((2,2-dioxido-2-thia-6-azaspiro[3.3]heptan-6-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

55) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((tetrahydro-1H-furo[3,4-c]pyrrol-5(3H)-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

56) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

57) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((((1R,2R)-2-hydroxycyclopentyl)(methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

58) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((3-((2-hydroxyethyl)amino)propyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

59) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((2-(dimethylamino)ethyl)(methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

60) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((2-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

61) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

62) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((2,2-dimethylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

63) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((S)-2-(methoxymethyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

64) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((((S)-tetrahydrofuran-2-yl)methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

65) ((2-(2'-cyano-3'-(6-(difluoromethoxy)-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline;

66) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-D-proline;

67) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3,3-dimethylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

68) ((2-(3'-(5-((3-(diethylamino)azetidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

69) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-(2-hydroxypropan-2-yl)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

70) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((2,5-dihydro-1H-pyrrol-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

71) ((2-(3'-(5-((2-azabicyclo[2.1.1]hexan-2-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

72) ((2-(3'-(5-(((1s,4s)-7-azabicyclo[2.2.1]heptan-7-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

73) ((2-(3'-(5-((((3,3-difluoro-1-(hydroxymethyl)cyclobutyl)methyl)amino)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

74) ((2-(3'-(5-((5-azaspiro[2.3]hexan-5-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

75) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-oxo-6-azabicyclo[3.2.1]octan-6-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

76) ((2-(3'-(5-((1,1-difluoro-5-azaspiro[2.3]hexan-5-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

77) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-(hydroxymethyl)-3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

78) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-(hydroxymethyl)-3-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

79) ((2-(3'-(5-((3-cyano-3-methylazetidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

80) ((2-(3'-(5-((3-cyanoazetidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

81) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-methyleneazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

82) ((2-(3'-(5-((3-(cyanomethylene)azetidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

83) ((2-(2,2'-dicyano-3'-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

84) ((6-(difluoromethoxy)-2-(3'-(5-((3,4-dimethylpyrrolidin-1-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

85) (R)-1-((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid;

86) (S)-1-((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid;

87) ((2-(2'-cyano-3'-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline;

88) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((3-methylpyrrolidin-1-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

89) ((2-(3'-(5-((2-azabicyclo[2.1.1]hexan-2-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

90) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((3-methylpyrrolidin-1-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-D-proline;

91) (3R)-1-((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((3-methylpyrrolidin-1-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid;

92) (3S)-1-((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((3-methylpyrrolidin-1-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid;

93) ((6-(difluoromethoxy)-2-(3'-(5-((3,3-dimethylazetidin-1-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

94) ((2-(3'-(5-(azetidin-1-ylmethyl)-7-methylbenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

95) ((6-(difluoromethoxy)-2-(3'-(7-fluoro-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

96) ((6-(difluoromethoxy)-2-(3'-(5-((ethylamino)methyl)-6-fluorobenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

97) ((2-(3'-(6-chloro-5-((ethylamino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

98) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

99) ((6-(difluoromethoxy)-2-(3'-(5-((((1R,2S)-2-hydroxycyclopentyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

100) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

101) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)-6-(trifluoromethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

102) ((2-(3'-(6,7-difluoro-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

103) ((2-(3'-(7-cyano-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

104) ((6-(difluoromethoxy)-2-(3'-(5-((2-hydroxy-2-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

105) ((6-(difluoromethoxy)-2-(3'-(5-((2-(hydroxymethyl)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

106) ((2-(3'-(5-((6-oxa-1-azaspiro[3.3]heptan-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

107) ((2-(3'-(5-((1-azaspiro[3.3]heptan-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

108) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(6-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

109) ((6-(difluoromethoxy)-2-(3'-(6-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

110) ((2-(2'-chloro-3'-(6-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

111) ((2-(2'-chloro-3'-(6-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline;

112) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(6-(pyrrolidin-1-ylmethyl)oxazolo[5,4-b]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

113) ((6-(difluoromethoxy)-2-(3'-(6-((3,3-dimethylazetidin-1-yl)methyl)oxazolo[5,4-b]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

114) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(6-(((R)-3-methylpyrrolidin-1-yl)methyl)oxazolo[5,4-b]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

115) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(6-((((5-oxopyrrolidin-2-yl)methyl)amino)methyl)oxazolo[5,4-b]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

116) ((6-(difluoromethoxy)-2-(3'-(6-((3-(dimethylamino)azetidin-1-yl)methyl)oxazolo[5,4-b]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

117) ((2-(3'-(6,7-difluoro-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2'-methoxy-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

118) ((2-(2'-cyano-3'-(6,7-difluoro-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

119) ((2-(3'-(6-((6-cyanopyridin-3-yl)methoxy)-5-(((2-hydroxyethyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

120) ((2-(3'-(6-((5-cyanopyridin-3-yl)methoxy)-5-(((2-hydroxyethyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

121) ((6-(difluoromethoxy)-2-(3'-(5-(((2-hydroxyethyl)amino)methyl)-6-((5-(methylsulfonyl)pyridin-3-yl)methoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

122) ((6-(difluoromethoxy)-2-(3'-(5-((ethylamino)methyl)-6-((5-(methylsulfonyl)pyridin-3-yl)methoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

123) ((6-(difluoromethoxy)-2-(3'-(5-((dimethylamino)methyl)-6-((5-(methylsulfonyl)pyridin-3-yl)methoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

124) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((methylamino)methyl)-6-((3-(methylsulfonyl)benzyl)oxy)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

125) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((methylamino)methyl)-6-((4-(methylsulfonyl)benzyl)oxy)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

126) ((6-(difluoromethoxy)-2-(3'-(5-((dimethylamino)methyl)-6-((4-(methylsulfonyl)benzyl)oxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

127) ((2-(3'-(7-cyano-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

128) ((2-(2-cyano-3'-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2'-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

129) ((2-(3'-(7-cyano-5-((3-(hydroxymethyl)-3-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

130) ((2-(3'-(7-cyano-5-(((S)-3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

131) ((2-(3'-(7-cyano-5-(((R)-3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

132) ((2-(3'-(7-cyano-5-(((R)-3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline;

133) ((2-(3'-(7-cyano-5-(((3-methyloxetan-3-yl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

134) ((2-(3'-(7-cyano-5-((3-(dimethylamino)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

135) ((2-(3'-(7-cyano-5-((2-(2-hydroxyethyl)piperidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

136) ((2-(3'-(7-cyano-5-(((cyanomethyl)(methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

137) ((2-(3'-(7-cyano-5-((3-(hydroxymethyl)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

138) ((2-(3'-(7-cyano-5-(((2-hydroxy-2-methylpropyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

139) ((2-(3'-(7-cyano-5-((((5-oxopyrrolidin-2-yl)methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

140) ((2-(3'-(7-cyano-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline;

141) ((2-(3'-(7-cyano-5-((ethyl(2-hydroxyethyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

142) ((2-(3'-(7-cyano-5-((3-cyanopyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

143) ((2-(3'-(7-cyano-5-((3-cyanopyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline;

144) ((2-(3'-(7-cyano-5-((3-ethynyl-3-hydroxyazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

145) ((2-(3'-(7-cyano-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline;

146) ((2-(3'-(7-cyano-5-((7-oxo-2,6-diazaspiro[3.4]octan-2-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

147) ((2-(3'-(5-((bis(1-hydroxypropan-2-yl)amino)methyl)-7-cyanobenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

148) ((2-(3'-(7-cyano-5-((3-morpholinoazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

149) ((2-(3'-(7-cyano-5-((3-(methyl(oxetan-3-yl)amino)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

150) ((2-(3'-(7-cyano-5-((3-hydroxy-3-methyl-[1,3'-biazetidin]-1'-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

151) ((2-(3'-(7-cyano-5-((6-oxo-2,5-diazaspiro[3.4]octan-2-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

152) ((2-(3'-(7-cyano-5-((3-((dimethylamino)methyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

153) ((2-(3'-(7-cyano-5-((1,1-difluoro-5-azaspiro[2.4]heptan-5-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

154) ((2-(3'-(7-cyano-5-(((R)-3-(hydroxymethyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

155) ((2-(3'-(7-cyano-5-(((3-hydroxycyclobutyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

156) ((2-(3'-(5-((3-amino-4-methylpyrrolidin-1-yl)methyl)-7-cyanobenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

157) ((2-(3'-(5-(((azetidin-3-ylmethyl)amino)methyl)-7-cyanobenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

158) ((2-(3'-(7-cyano-5-((3-(dimethylamino)-4-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

159) ((2-(3'-(7-cyano-5-((3-((dimethylamino)methyl)-3-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

160) ((2-(3'-(7-cyano-5-((((1-methyl-1H-imidazol-4-yl)methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

161) ((2-(3'-(5-((3-(aminomethyl)-3-methylazetidin-1-yl)methyl)-7-cyanobenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

162) ((2-(3'-(7-cyano-5-((3-fluoropyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

163) ((2-(3'-(7-cyano-5-((3-fluoropyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline;

164) ((2-(3'-(7-cyano-5-((3,4-difluoropyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

165) ((2-(3'-(7-cyano-5-(((R)-3-cyanopyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

166) ((6-(difluoromethoxy)-2-(3'-(5-((3-fluoropyrrolidin-1-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

167) ((2-(3'-(7-cyano-5-((3-fluoro-3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

168) ((2-(3'-(7-cyano-5-(((R)-3-(fluoromethyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

169) (R)-1-((2-(3'-(7-cyano-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid;

170) ((6-(difluoromethoxy)-2-(3'-(6-((3,3-dimethylazetidin-1-yl)methyl)oxazolo[5,4-b]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-D-proline;

171) S)-1-((8-((3'-(5-(((S)-2-carboxypyrrolidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)amino)-1,7-naphthyridin-3-yl)methyl)-2-methylpyrrolidine-2-carboxylic acid;

172) ((2-(3'-((3-(((carboxymethyl)amino)methyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

173) (S)-1-((8-((3'-(5-(((S)-2-carboxypyrrolidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)amino)-1,7-naphthyridin-3-yl)methyl)piperidine-2-carboxylic acid;

174) ((6-(difluoromethoxy)-2-(3'-((3-((3-fluoropyrrolidin-1-yl)methyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

175) ((6-(difluoromethoxy)-2-(3'-((3-((3-hydroxypyrrolidin-1-yl)methyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

176) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-((3-(morpholinomethyl)-1,7-naphthyridin-8-yl)amino)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

177) ((2-(3'-((3-(azetidin-1-ylmethyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline;

178) ((6-(difluoromethoxy)-2-(3'-((3-((3-hydroxyazetidin-1-yl)methyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

179) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-((3-((((5-oxopyrrolidin-2-yl)methyl)amino)methyl)-1,7-naphthyridin-8-yl)amino)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

180) (3S)-1-((6-(difluoromethoxy)-2-(3'-((3-((3-hydroxypyrrolidin-1-yl)methyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid;

181) (3R)-1-((6-(difluoromethoxy)-2-(3'-((3-((3-hydroxypyrrolidin-1-yl)methyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid;

182) ((6-(difluoromethoxy)-2-(3'-((3-((3-hydroxypyrrolidin-1-yl)methyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-D-proline;

183) ((5-(difluoromethoxy)-2-(2,2'-dimethyl-3'-((4-(pyrrolidin-1-ylmethyl)pyridin-2-yl)amino)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-6-yl)methyl)-L-proline;

184) ((2-(3'-(5-(carboxymethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

185) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(2-(methylsulfonyl)ethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

186) ((2-(3'-(5-(1-carboxyethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

187) ((2-(3'-(5-(2-carboxyethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

188) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-methyl-4,5,6,7-tetrahydrooxazolo[5,4-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

189) ((6-(difluoromethoxy)-2-(3'-(5-(2-hydroxyethyl)-4,5,6,7-tetrahydrooxazolo[5,4-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

190) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

191) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(4,4,4-trifluorobutyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

192) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(oxetan-2-ylmethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

193) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((5-oxopyrrolidin-2-yl)methyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

194) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyridin-3-ylmethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

195) ((2-(3'-(5-(cyanomethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline;

196) ((2-(3'-(5-(2-amino-2-oxoethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline;

197) ((6-(difluoromethoxy)-2-(3'-(5-(ethylsulfonyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

198) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(3,3,3-trifluoropropyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

199) ((6-(difluoromethoxy)-2-(3'-(5-(3-hydroxypropyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

200) ((6-(difluoromethoxy)-2-(3'-(5-(3-fluoropropyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

201) ((2-(3'-(5-(2,2-difluoroethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline;

202) ((6-(difluoromethoxy)-2-(3'-(5,6-dihydro-4H-pyrrolo[3,4-d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

203) ((6-(difluoromethoxy)-2-(3'-(6,7-dihydro-4H-pyrano[3,4-d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

204) ((6-(difluoromethoxy)-2-(3'-(5,6-dihydro-4H-cyclopenta[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

205) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(4,5,6,7-tetrahydrobenzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

206) ((6-(difluoromethoxy)-2-(3'-(5-(2-hydroxyethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

207) 2-((2-(2'-cyano-2-methyl-3'-(4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)pyrrolidine-1-carboxylic acid;

208) ((2-(3'-((2-chloro-5-((5-(difluoromethoxy)pyridin-3-yl)methoxy)-4-(((R)-3-hydroxypyrrolidin-1-yl)methyl)phenoxy)methyl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

209) ((2-(3'-((2-chloro-5-((5-(difluoromethoxy)pyridin-3-yl)methoxy)-4-((3-fluoropyrrolidin-1-yl)methyl)phenoxy)methyl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

210) ((2-(3'-((4-(((2-acetamidoethyl)amino)methyl)-2-chloro-5-((3-cyanobenzyl)oxy)phenoxy)methyl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

211) ((2-(3'-((4-(((S)-2-carboxypyrrolidin-1-yl)methyl)-2-chloro-5-((3-cyanobenzyl)oxy)phenoxy)methyl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

212) ((6-(difluoromethoxy)-2-(3'-(((4,6-dimethoxy-5-(pyrrolidin-1-ylmethyl)pyrimidin-2-yl)oxy)methyl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

213) ((6-(difluoromethoxy)-2-(3'-(((5-((3,3-dimethylazetidin-1-yl)methyl)-4,6-dimethoxypyrimidin-2-yl)oxy)methyl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

214) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-((5-(((((S)-5-oxopyrrolidin-2-yl)methyl)amino)methyl)pyridin-2-yl)oxy)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

215) ((6-(difluoromethoxy)-2-(2'-fluoro-2-methyl-4"-(((((S)-5-oxopyrrolidin-2-yl)methyl)amino)methyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

216) ((6-(difluoromethoxy)-2-(3"-(difluoromethoxy)-2'-fluoro-2-methyl-4"-(((((S)-5-oxopyrrolidin-2-yl)methyl)amino)methyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

217) ((6-(difluoromethoxy)-2-(4"-(((2-hydroxyethyl)amino)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

218) ((6-(difluoromethoxy)-2-(2,2',3"-trimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

219) ((2-(3"-chloro-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline;

220) ((6-(difluoromethoxy)-2-(2"-fluoro-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

221) ((2-(2'-bromo-2"-fluoro-2-methyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline;

222) ((2-(2'-chloro-2"-fluoro-2-methyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline;

223) ((2-(2'-chloro-2"-fluoro-2-methyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

224) ((2-(2'-chloro-2"-fluoro-2-methyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline;

225) ((6-(difluoromethoxy)-2-(4"-guanidino-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

226) ((6-(difluoromethoxy)-2-(4"-(((3-(dimethylamino)propyl)(methyl)amino)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

227) ((6-(difluoromethoxy)-2-(4"-((3-methoxypyrrolidin-1-yl)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

228) ((6-(difluoromethoxy)-2-(4"-((3-(dimethylamino)pyrrolidin-1-yl)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

229) ((2-(3"-chloro-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

230) ((6-(difluoromethoxy)-2-(2,2',3"-trimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

231) ((2-(2"-chloro-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

232) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-3"-(trifluoromethoxy)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

233) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-3"-(trifluoromethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

234) ((6-(difluoromethoxy)-2-(2,2',3",5"-tetramethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

235) ((6-(difluoromethoxy)-2-(3"-fluoro-5"-methoxy-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

236) ((2-(3"-carboxy-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

237) ((6-(difluoromethoxy)-2-(4"-((3,3-dimethylazetidin-1-yl)methyl)-3"-fluoro-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

238) ((6-(difluoromethoxy)-2-(3"-fluoro-2,2'-dimethyl-4"-((3-methylpyrrolidin-1-yl)methyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

239) ((6-(difluoromethoxy)-2-(3"-fluoro-4"-(((2-hydroxyethyl)amino)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

240) ((2-(3"-cyano-4"-(((S)-3-(hydroxymethyl)pyrrolidin-1-yl)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

241) ((6-(difluoromethoxy)-2-(3"-fluoro-4"-(isoindolin-2-ylmethyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

242) ((6-(difluoromethoxy)-2-(4"-((3-fluoropyrrolidin-1-yl)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

243) ((6-(difluoromethoxy)-2-(3"-fluoro-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

244) ((6-(difluoromethoxy)-2-(3"-(difluoromethoxy)-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

245) ((2-(3"-cyano-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

246) ((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(((S)-3-methylpyrrolidin-1-yl)methyl)pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

247) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(2-((S)-pyrrolidin-2-yl)-1H-imidazol-4-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

248) ((6-(difluoromethoxy)-2-(3"-fluoro-2,2'-dimethyl-4"-(((S)-3-phenylpyrrolidin-1-yl)methyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

249) ((6-(difluoromethoxy)-2-(3"-(4-fluorophenethoxy)-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

250) ((2-(3"-(cyclopropylmethoxy)-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline;

251) ((2-(4"-(((R)-3-(1H-tetrazol-5-yl)pyrrolidin-1-yl)methyl)-3"-fluoro-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline;

252) ((2-(4"-(((S)-3-((benzyloxy)methyl)pyrrolidin-1-yl)methyl)-3"-fluoro-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline;

253) ((6-(difluoromethoxy)-2-(2"-fluoro-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

254) ((6-(difluoromethoxy)-2-(3",5"-dimethoxy-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline hydrochloride;

255) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-4"-(pyrrolidin-2-yl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

256) ((2-(4"-((S)-amino(carboxy)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

257) ((6-(difluoromethoxy)-2-(4"-(((S)-3-((S)-2-((methoxycarbonyl)amino)-3-methylbutanamido)pyrrolidin-1-yl)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

258) ((6-(difluoromethoxy)-2-(3"-fluoro-2,2'-dimethyl-4"-((5-ureidoisoindolin-2-yl)methyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

259) (S)-1-((2-(3'-(7-cyano-5-(((S)-3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid;

260) ((6-(difluoromethoxy)-2-(3"-fluoro-2,2'-dimethyl-4"-((3-ureidopyrrolidin-1-yl)methyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

261) ((2-(3'-(5-(((S)-3-chloropyrrolidin-1-yl)methyl)-7-cyanobenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

262) ((6-(difluoromethoxy)-2-(3'-(4-fluoro-6-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

263) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(6-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

264) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

265) ((6-(difluoromethoxy)-2-(3'-(5-fluoro-6-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

266) ((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(pyrrolidin-1-ylmethyl)pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

267) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(6-oxo-5-(pyrrolidin-1-ylmethyl)-1,6-dihydropyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

268) ((6-(difluoromethoxy)-2-(2'-(difluoromethyl)-3'-(5-fluoro-6-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-2-methyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

269) ((6-(difluoromethoxy)-2-(3'-(5-fluoro-6-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-2'-(fluoromethyl)-2-methyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

270) ((6-(difluoromethoxy)-2-(3'-(2-fluoro-6-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

271) ((6-(difluoromethoxy)-2-(3'-(5-((3,3-dimethylazetidin-1-yl)methyl)-6-methoxypyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

272) ((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(((R)-3-methylpyrrolidin-1-yl)methyl)pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

273) ((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(((S)-3-methylpyrrolidin-1-yl)methyl)pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-D-proline;

274) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)-4-vinylpyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

275) ((6-(difluoromethoxy)-2-(3'-(5-((3-(difluoromethyl)pyrrolidin-1-yl)methyl)-6-methoxypyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

276) ((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-((((5-oxopyrrolidin-2-yl)methyl)amino)methyl)pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

277) ((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(((S)-2-methylpyrrolidin-1-yl)methyl)pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

278) ((2-(3'-(5-(((1s,4s)-7-azabicyclo[2.2.1]heptan-7-yl)methyl)-6-methoxypyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

279) ((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(((R)-2-methylpyrrolidin-1-yl)methyl)pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

280) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)thiophen-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

281) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(2-(pyrrolidin-1-ylmethyl)pyrimidin-5-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline

282) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(2-(4-methylpiperazin-1-yl)pyrimidin-5-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

283) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(2-(pyrrolidin-1-yl)pyrimidin-5-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

284) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)pyrazin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

285) ((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(pyrrolidin-1-ylmethyl)pyrazin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

286) ((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(((R)-3-methylpyrrolidin-1-yl)methyl)pyrazin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

287) ((2-(2'-chloro-3'-(6-methoxy-5-((((5-oxopyrrolidin-2-yl)methyl)amino)methyl)pyrazin-2-yl)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

288) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(1,2,3,4-tetrahydroisoquinolin-6-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

289) ((6-(difluoromethoxy)-2-(3'-(isoindolin-5-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

290) ((2-(3'-(2-(2-carboxyethyl)isoindolin-5-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

291) ((2-(3'-(2-(carboxymethyl)isoindolin-5-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

292) ((2-(3'-(2-(1-carboxyethyl)isoindolin-5-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

293) ((2-(3'-(2-amino-1H-benzo[d]imidazol-5-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

294) ((6-(difluoromethoxy)-2-(3'-(5-((3,3-dimethylpyrrolidin-1-yl)methyl)-6-methoxypyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

295) ((2-(3'-(7-cyano-5-(pyrrolidin-1-ylmethyl)-1H-benzo[d]imidazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

296) ((2-(3'-(6,7-difluoro-5-(pyrrolidin-1-ylmethyl)-1H-benzo[d]imidazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

297) ((6-(difluoromethoxy)-2-(3'-(6-fluoro-5-(pyrrolidin-1-ylmethyl)-1H-benzo[d]imidazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

298) ((2-(3'-(6,7-difluoro-1-methyl-5-(pyrrolidin-1-ylmethyl)-1H-benzo[d]imidazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

299) ((2-(3'-(6,7-difluoro-5-(pyrrolidin-1-ylmethyl)-1-(2,2,2-trifluoroethyl)-1H-benzo[d]imidazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

300) ((2-(3'-(4,5-difluoro-6-(pyrrolidin-1-ylmethyl)-1-(2,2,2-trifluoroethyl)-1H-benzo[d]imidazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

301) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)-7-(trifluoromethyl)-1H-benzo[d]imidazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

302) ((2-(2'-chloro-3'-(5-(((2-hydroxyethyl)amino)methyl)picolinamido)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

303) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine-2-carboxamido)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

304) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(4-methyl-5-(pyrrolidin-1-ylmethyl)oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

305) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(6-(pyrrolidin-1-ylmethyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

306) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(4-(pyrrolidin-1-yl)piperidin-1-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

307) ((6-(difluoromethoxy)-2-(3'-(4-(((1-(hydroxymethyl)cyclopropyl)methyl)amino)piperidin-1-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

308) ((6-(difluoromethoxy)-2-(3'-(4-((3,3-dimethylazetidin-1-yl)methyl)piperidin-1-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

309) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(4-(pyrrolidin-1-ylmethyl)piperidin-1-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

310) ((6-(difluoromethoxy)-2-(3'-(5-((((1R,2S)-2-hydroxycyclopentyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-D-proline;

311) ((6-(difluoromethoxy)-2-(3'-(5-((2,2-dimethylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

312) ((6-(difluoromethoxy)-2-(3'-(5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

313) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((2-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

314) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-methyl-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

315) ((2-(3'-(5-((3-carbamoylpyrrolidin-1-yl)methyl)-7-cyanobenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline; or

316) ((2-(3'-(7-cyano-5-((3-cyano-3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline.

The present invention also provides a pharmaceutical composition comprising a compound of any of the present invention and a pharmaceutically acceptable excipient, such as hydroxypropyl methyl cellulose. In the composition, the said compound in a weight ratio to the said excipient within the range from about 0.0001 to about 10.

The present invention additionally provided a use of a pharmaceutical composition of Formula I for the preparation of a medicament for treating a disease in a subject.

The present invention further provides some preferred technical solutions with regard to above-mentioned uses.

In some embodiments, a medicament thus prepared can be used for the treatment or prevention of, or for delaying or preventing onset or progression in, cancer, cancer metastasis, an immunological disorder. The cancer is colon cancer, gastric cancer, thyroid cancer, lung cancer, leukemia, pancreatic cancer, melanoma, multiple melanoma, brain cancer, renal cancer, prostate cancer, ovarian cancer or breast cancer.

The present invention provided a method of inhibiting PD-1/PD-L1 interaction, said method comprising administering to a patient a compound, or a pharmaceutically acceptable salt or a stereoisomer thereof.

The present invention provided a method of treating a disease associated with inhibition of PD-1/PD-L1 interaction, said method comprising administering to a patient in need thereof a therapeutically effective amount of a compound of the present invention, or a pharmaceutically acceptable salt or a stereoisomer thereof. Wherein the disease is colon cancer, gastric cancer, thyroid cancer, lung cancer, leukemia, pancreatic cancer, melanoma, multiple melanoma, brain cancer, renal cancer, prostate cancer, ovarian cancer, or breast cancer.

The present invention provided a method of enhancing, stimulating and/or increasing the immune response in a patient, said method comprising administering to the patient in need thereof a therapeutically effective amount of a compound of the present invention, or a pharmaceutically acceptable salt or a stereoisomer thereof.

The present invention also provides a use of the present compound or its pharmaceutical composition for the preparation of a medicament.

In some embodiments, the medicament is used for the treatment or prevention of cancer.

In some embodiments, the cancer is colon cancer, gastric cancer, thyroid cancer, lung cancer, leukemia, pancreatic cancer, melanoma, multiple melanoma, brain cancer, renal cancer, prostate cancer, ovarian cancer or breast cancer.

In some embodiments, the medicament is used as an inhibitor of PD-1/PD-L1 interaction.

In some embodiments, the medicament is used for enhancing, stimulating and/or increasing the immune response in a patient.

The general chemical terms used in the formula above have their usual meanings. For example, the term “halogen”, as used herein, unless otherwise indicated, means fluoro, chloro, bromo or iodo. The preferred halogen groups include F, Cl and Br.

As used herein, unless otherwise indicated, alkyl includes saturated monovalent hydrocarbon radicals having straight, branched or cyclic moieties. For example, alkyl radicals include methyl, ethyl, propyl, isopropyl, cyclcopropyl, n-butyl, isobutyl, sec-butyl, t-butyl, cyclcobutyl, n-pentyl, 3- (2-methyl) butyl, 2-pentyl, 2-methylbutyl, neopentyl, cyclcopentyl, n-hexyl, 2-hexyl, 2-methylpentyl and cyclohexyl. Similary, C_{1-4}, as in C_{1-4}alkyl is defined to identify the group as having 1, 2, 3, or 4 carbon atoms in a linear or branched arrangement.

Alkenyl and alkynyl groups include straight, branched chain or cyclic alkenes and alkynes. Likewise, “C_{2-8} alkenyl” and “C_{2-8} alkynyl” means an alkenyl or alkynyl radicals having 2, 3, 4, 5, 6, 7 or 8 carbon atoms in a linear or brached arrangement.

Alkoxy radicals are oxygen ethers formed from the previously described straight, branched chain or cyclic alkyl groups.

The term "aryl", as used herein, unless otherwise indicated, refers to an unsubstituted or substituted mono- or polycyclic ring system containing carbon ring atoms. The preferred aryls are mono cyclic or bicyclic 6-10 membered aromatic ring systems. Phenyl and naphthyl are preferred aryls. The most preferred aryl is phenyl.

The term "heterocyclyl", as used herein, unless otherwise indicated, represents an unsubstituted or substituted stable three to ten membered saturated or partially unsaturated monocyclic, spirocyclic, bridged bicyclic or fused bicyclic ring system which consists of carbon atoms and one to three heteroatoms selected from N, O or S, and wherein the nitrogen or sulfur heteroatoms may optionally be oxidized, and the nitrogen heteroatom may optionally be quaternized. The heterocyclyl group may be attached at any heteroatom or carbon atom which results in the creation of a stable structure. Examples of such heterocyclyl groups include, but are not limited to azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, oxopiperazinyl, oxopiperidinyl, oxoazepinyl, azepinyl, tetrahydrofuranyl, dioxolanyl, tetrahydroimidazolyl, tetrahydrothiazolyl, tetrahydrooxazolyl, tetrahydropyranyl, morpholinyl, thiomorpholinyl, thiamorpholinyl sulfoxide, thiamorpholinyl sulfone and oxadiazolyl.

The term "heteroaryl", as used herein, unless otherwise indicated, represents an unsubstituted or substituted stable five or six membered monocyclic aromatic ring system or an unsubstituted or substituted nine or ten membered benzo-fused heteroaromatic ring system or bicyclic heteroaromatic ring system which consists of carbon atoms and from one to four heteroatoms selected from N, O or S, and wherein the nitrogen or sulfur heteroatoms may optionally be oxidized, and the nitrogen heteroatom may optionally be quaternized. The heteroaryl group may be attached at any heteroatom or carbon atom which results in the creation of a stable structure. Examples of heteroaryl groups include, but are not limited to thienyl, furanyl, imidazolyl, isoxazolyl, oxazolyl, pyrazolyl, pyrrolyl, thiazolyl, thiadiazolyl, triazolyl, pyridyl, pyridazinyl, indolyl, azaindolyl, indazolyl, benzimidazolyl, benzofuranyl, benzothienyl, benzisoxazolyl, benzoxazolyl, benzopyrazolyl, benzothiazolyl, benzothiadiazolyl, benzotriazolyl adeninyl, quinolinyl or isoquinolinyl.

The term "alkenyloxy" refers to the group -O-alkenyl, where alkenyl is defined as above.

The term "alknyloxy" refers to the group -O-alknyl, where alknyl is defined as above.

The term "cycloalkyl" to a cyclic saturated alkyl chain having from 3 to 12 carbon atoms, for example, cyclopropyl, cyclobutyl, cyclobutyl, cyclobutyl.

The term "substituted" refers to a group in which one or more hydrogen atoms are each

independently replaced with the same or different substituent(s). Typical substituents include, but are not limited to, halogen (F, Cl, Br or I), C_{1-8} alkyl, C_{3-12} cycloalkyl, $-OR^1$, SR^1, =O, =S, $-C(O)R^1$, $-C(S)R^1$, $=NR^1$, $-C(O)OR^1$, $-C(S)OR^1$, $-NR^1R^2$, $-C(O)NR^1R^2$, cyano, nitro, $-S(O)_2R^1$, $-OS(O_2)OR^1$, $-OS(O)_2R^1$, $-OP(O)(OR^1)(OR^2)$; wherein R^1 and R^2 is independently selected from -H, lower alkyl, lower haloalkyl. In some embodiments, the substituent(s) is independently selected from the group consisting of -F, -Cl, -Br, -I, -OH, trifluromethoxy, ethoxy, propyloxy, iso-propyloxy, n-butyloxy, isobutyloxy, t-butyloxy, $-SCH_3$, $-SC_2H_5$, formaldehyde group, $-C(OCH_3)$, cyano, nitro, CF_3,$-OCF_3$, amino, dimethylamino, methyl thio, sulfonyl and acetyl.

The term “composition”, as used herein, is intended to encompass a product comprising the specified ingredients in the specified amounts, as well as any product which results, directly or indirectly, from combinations of the specified ingredients in the specified amounts. Accordingly, pharmaceutical compositions containing the compounds of the present invention as the active ingredient as well as methods of preparing the instant compounds are also part of the present invention. Furthermore, some of the crystalline forms for the compounds may exist as polymorphs and as such are intended to be included in the present invention. In addition, some of the compounds may form solvates with water (i.e., hydrates) or common organic solvents and such solvates are also intended to be encompassed within the scope of this invention.

Examples of substituted alkyl group include, but not limited to, 2-aminoethyl, 2-hydroxyethyl, pentachloroethyl, trifluoromethyl, methoxymethyl, pentafluoroethyl and piperazinylmethyl.

Examples of substituted alkoxy groups include, but not limited to, aminomethoxy, thrifluoromethoxy, 2-diethylaminoethoxy, 2-ethoxycarbonylethoxy, 3-hydroxypropoxy.

The compounds of the present invention may also be present in the form of pharmaceutically acceptable salts. For use in medicine, the salts of the compounds of this invention refer to non-toxic “pharmaceutically acceptable salts”. The pharmaceutically acceptable salt forms include pharmaceutically acceptable acidic/anionic or basic/cationic salts. The pharmaceutically acceptable acidic/anionic salt generally takes a form in which the basic nitrogen is protonated with an inorganic or organic acid. Representative organic or inorganic acids include hydrochloric, hydrobromic, hydriodic, perchloric, sulfuric, nitric, phosphoric, acetic, propionic, glycolic, lactic, succinic, maleic, fumaric, malic, tartaric, citric, benzoic, mandelic, methanesulfonic, hydroxyethanesulfonic, benzenesulfonic, oxalic, pamoic, 2-naphthalenesulfonic, p-toluenesulfonic, cyclohexanesulfamic, salicylic, saccharinic or trifluoroacetic. Pharmaceutically acceptable basic/cationic salts include, and are not limited to

aluminum, calcium, chloroprocaine, choline, diethanolamine, ethylenediamine, lithium, magnesium, potassium, sodium and zinc.

The present invention includes within its scope the prodrugs of the compounds of this invention. In general, such prodrugs will be functional derivatives of the compounds that are readily converted in vivo into the required compound. Thus, in the methods of treatment of the present invention, the term "administering" shall encompass the treatment of the various disorders described with the compound specifically disclosed or with a compound which may not be specifically disclosed, but which converts to the specified compound in vivo after administration to the subject. Conventional procedures for the selection and preparation of suitable prodrug derivatives are described, for example, in "Design of Prodrugs", ed. H. Bundgaard, Elsevier, 1985.

It is intended that the definition of any substituent or variable at a particular location in a molecule be independent of its definitions elsewhere in that molecule. It is understood that substituents and substitution patterns on the compounds of this invention can be selected by one of ordinary skill in the art to provide compounds that are chemically stable and that can be readily synthesized by techniques know in the art as well as those methods set forth herein.

The present invention includes compounds described herein can contain one or more asymmetric centers and may thus give rise to diastereomers and optical isomers. The present invention includes all such possible diastereomers as well as their racemic mixtures, their substantially pure resolved enantiomers, all possible geometric isomers, and pharmaceutically acceptable salts thereof.

The above Formula I are shown without a definitive stereochemistry at certain positions. The present invention includes all stereoisomers of Formula I and pharmaceutically acceptable salts thereof. Further, mixtures of stereoisomers as well as isolated specific stereoisomers are also included. During the course of the synthetic procedures used to prepare such compounds, or in using racemization or epimerization procedures known to those skilled in the art, the products of such procedures can be a mixture of stereoisomers.

When a tautomer of the compound of Formula I exists, the present invention includes any possible tautomers and pharmaceutically acceptable salts thereof, and mixtures thereof, except where specifically stated otherwise.

When the compound of Formula I and pharmaceutically acceptable salts thereof exist in the form of solvates or polymorphic forms, the present invention includes any possible solvates and polymorphic forms. A type of a solvent that forms the solvate is not particularly limited so long

as the solvent is pharmacologically acceptable. For example, water, ethanol, propanol, acetone or the like can be used.

The term "pharmaceutically acceptable salts" refers to salts prepared from pharmaceutically acceptable non-toxic bases or acids. When the compound of the present invention is acidic, its corresponding salt can be conveniently prepared from pharmaceutically acceptable non-toxic bases, including inorganic bases and organic bases. Salts derived from such inorganic bases include aluminum, ammonium, calcium, copper (ic and ous), ferric, ferrous, lithium, magnesium, manganese (ic and ous), potassium, sodium, zinc and the like salts. Particularly preferred are the ammonium, calcium, magnesium, potassium and sodium salts. Salts derived from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary, and tertiary amines, as well as cyclic amines and substituted amines such as naturally occurring and synthesized substituted amines. Other pharmaceutically acceptable organic non-toxic bases from which salts can be formed include ion exchange resins such as, for example, arginine, betaine, caffeine, choline, *N*',*N*'- dibenzylethylenediamine, diethylamine, 2-diethylaminoethanol, 2-dimethylaminoethanol, ethanolamine, ethylenediamine, N-ethylmorpholine, N-ethylpiperidine, glucamine, glucosamine, histidine, hydrabamine, isopropylamine, lysine, methylglucamine, morpholine, piperazine, piperidine, polyamine resins, procaine, purines, theobromine, triethylamine, trimethylamine, tripropylamine, tromethamine and the like.

When the compound of the present invention is basic, its corresponding salt can be conveniently prepared from pharmaceutically acceptable non-toxic acids, including inorganic and organic acids. Such acids include, for example, acetic, benzenesulfonic, benzoic, camphorsulfonic, citric, ethanesulfonic, formic, fumaric, gluconic, glutamic, hydrobromic, hydrochloric, isethionic, lactic, maleic, malic, mandelic, methanesulfonic, mucic, nitric, pamoic, pantothenic, phosphoric, succinic, sulfuric, tartaric, p-toluenesulfonic acid and the like. Preferred are citric, hydrobromic, formic, hydrochloric, maleic, phosphoric, sulfuric and tartaric acids, particularly preferred are formic and hydrochloric acid. Since the compounds of Formula I are intended for pharmaceutical use they are preferably provided in substantially pure form, for example at least 60% pure, more suitably at least 75% pure, especially at least 98% pure (% are on a weight for weight basis).

The pharmaceutical compositions of the present invention comprise a compound represented by Formula I (or a pharmaceutically acceptable salt thereof) as an active ingredient, a pharmaceutically acceptable carrier and optionally other therapeutic ingredients or adjuvants. The compositions include compositions suitable for oral, rectal, topical, and parenteral (including subcutaneous, intramuscular, and intravenous) administration, although the most

suitable route in any given case will depend on the particular host, and nature and severity of the conditions for which the active ingredient is being administered. The pharmaceutical compositions may be conveniently presented in unit dosage form and prepared by any of the methods well known in the art of pharmacy.

In practice, the compounds represented by Formula I, or a prodrug, or a metabolite, or pharmaceutically acceptable salts thereof, of this invention can be combined as the active ingredient in intimate admixture with a pharmaceutical carrier according to conventional pharmaceutical compounding techniques. The carrier may take a wide variety of forms depending on the form of preparation desired for administration, e.g., oral or parenteral (including intravenous). Thus, the pharmaceutical compositions of the present invention can be presented as discrete units suitable for oral administration such as capsules, cachets or tablets each containing a predetermined amount of the active ingredient. Further, the compositions can be presented as a powder, as granules, as a solution, as a suspension in an aqueous liquid, as a non-aqueous liquid, as oil-in-water emulsion, or as a water-in- oil liquid emulsion. In addition to the common dosage forms set out above, the compound represented by Formula I, or a pharmaceutically acceptable salt thereof, may also be administered by controlled release means and/or delivery devices. The compositions may be prepared by any of the methods of pharmacy. In general, such methods include a step of bringing into association the active ingredient with the carrier that constitutes one or more necessary ingredients. In general, the compositions are prepared by uniformly and intimately admixing the active ingredient with liquid carriers or finely divided solid carriers or both. The product can then be conveniently shaped into the desired presentation.

Thus, the pharmaceutical compositions of this invention may include a pharmaceutically acceptable carrier and a compound, or a pharmaceutically acceptable salt, of Formula I. The compounds of Formula I, or pharmaceutically acceptable salts thereof, can also be included in pharmaceutical compositions in combination with one or more other therapeutically active compounds.

The pharmaceutical carrier employed can be, for example, a solid, liquid, or gas. Examples of solid carriers include such as lactose, terra alba, sucrose, talc, gelatin, agar, pectin, acacia, magnesium stearate, and stearic acid. Examples of liquid carriers include such as sugar syrup, peanut oil, olive oil, and water. Examples of gaseous carriers include such as carbon dioxide and nitrogen. In preparing the compositions for oral dosage form, any convenient pharmaceutical media may be employed. For example, water, glycols, oils, alcohols, flavoring agents, preservatives, coloring agents, and the like may be used to form oral liquid preparations such as

suspensions, elixirs and solutions; while carriers such as starches, sugars, microcrystalline cellulose, diluents, granulating agents, lubricants, binders, disintegrating agents, and the like may be used to form oral solid preparations such as powders, capsules and tablets. Because of their ease of administration, tablets and capsules are the preferred oral dosage units whereby solid pharmaceutical carriers are employed. Optionally, tablets may be coated by standard aqueous or nonaqueous techniques.

A tablet containing the composition of this invention may be prepared by compression or molding, optionally with one or more accessory ingredients or adjuvants. Compressed tablets may be prepared by compressing, in a suitable machine, the active ingredient in a free-flowing form such as powder or granules, optionally mixed with a binder, lubricant, inert diluent, surface active or dispersing agent. Molded tablets may be made by molding in a suitable machine, a mixture of the powdered compound moistened with an inert liquid diluent. Each tablet preferably contains from about 0.05mg to about 5g of the active ingredient and each cachet or capsule preferably containing from about 0.05mg to about 5g of the active ingredient. For example, a formulation intended for the oral administration to humans may contain from about 0.5mg to about 5g of active agent, compounded with an appropriate and convenient amount of carrier material which may vary from about 5 to about 95 percent of the total composition. Unit dosage forms will generally contain between from about l mg to about 2g of the active ingredient, typically 25mg, 50mg, l00mg, 200mg, 300mg, 400mg, 500mg, 600mg, 800mg, or l000mg.

Pharmaceutical compositions of the present invention suitable for parenteral administration may be prepared as solutions or suspensions of the active compounds in water. A suitable surfactant can be included such as, for example, hydroxypropylcellulose. Dispersions can also be prepared in glycerol, liquid polyethylene glycols, and mixtures thereof in oils. Further, a preservative can be included to prevent the detrimental growth of microorganisms.

Pharmaceutical compositions of the present invention suitable for injectable use include sterile aqueous solutions or dispersions. Furthermore, the compositions can be in the form of sterile powders for the extemporaneous preparation of such sterile injectable solutions or dispersions. In all cases, the final injectable form must be sterile and must be effectively fluid for easy syringability. The pharmaceutical compositions must be stable under the conditions of manufacture and storage; thus, preferably should be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (e.g., glycerol, propylene glycol and liquid polyethylene glycol), vegetable oils, and suitable mixtures thereof.

Pharmaceutical compositions of the present invention can be in a form suitable for topical use such as, for example, an aerosol, cream, ointment, lotion, dusting powder, or the like. Further, the compositions can be in a form suitable for use in transdermal devices. These formulations may be prepared, utilizing a compound represented by Formula I of this invention, or a pharmaceutically acceptable salt thereof, via conventional processing methods. As an example, a cream or ointment is prepared by admixing hydrophilic material and water, together with about 5wt% to about 10wt% of the compound, to produce a cream or ointment having a desired consistency.

Pharmaceutical compositions of this invention can be in a form suitable for rectal administration wherein the carrier is a solid. It is preferable that the mixture forms unit dose suppositories. Suitable carriers include cocoa butter and other materials commonly used in the art. The suppositories may be conveniently formed by first admixing the composition with the softened or melted carrier(s) followed by chilling and shaping in molds.

In addition to the aforementioned carrier ingredients, the pharmaceutical formulations described above may include, as appropriate, one or more additional carrier ingredients such as diluents, buffers, flavoring agents, binders, surface-active agents, thickeners, lubricants, preservatives (including antioxidants) and the like. Furthermore, other adjuvants can be included to render the formulation isotonic with the blood of the intended recipient. Compositions containing a compound described by Formula I, or pharmaceutically acceptable salts thereof, may also be prepared in powder or liquid concentrate form.

Generally, dosage levels on the order of from about 0.01mg/kg to about 150mg/kg of body weight per day are useful in the treatment of the above-indicated conditions, or alternatively about 0.5mg to about 7g per patient per day. For example, colon cancer, rectal cancer, mantle cell lymphoma, multiple myeloma, breast cancer, prostate cancer, glioblastoma, squamous cell esophageal cancer, liposarcoma, T-cell lymphoma melanoma, pancreatic cancer, glioblastoma or lung cancer, may be effectively treated by the administration of from about 0.01 to 50mg of the compound per kilogram of body weight per day, or alternatively about 0.5mg to about 3.5g per patient per day.

It is understood, however, that lower or higher doses than those recited above may be required. Specific dose level and treatment regimens for any particular subject will depend upon a variety of factors, including the activity of the specific compound employed, the age, body weight, general health, sex, diet, time of administration, route of administration, rate of excretion, drug combination, the severity and course of the particular disease undergoing therapy, the subject disposition to the disease, and the judgment of the treating physician.

These and other aspects will become apparent from the following written description of the invention.

The following Examples are provided to better illustrate the present invention. All parts and percentages are by weight and all temperatures are degrees Celsius, unless explicitly stated otherwise.

The invention will be described in greater detail by way of specific examples. The following examples are offered for illustrative purposes, and are not intended to limit the invention in any manner. Those of skill in the art will readily recognize a variety of non-critical parameters which can be changed or modified to yield essentially the same results. The compounds of the Examples have been found to inhibit the activity of PD-1/PD-L1 protein/protein interaction according to at least one assay described herein.

Examples

Experimental procedures for compounds of the invention are provided below. Open Access Preparative LCMS Purification of some of the compounds prepared was performed on Waters mass directed fractionation systems. The basic equipment setup, protocols and control software for the operation of these systems have been described in detail in literature. See, e.g., Blom, "Two-Pump At Column Dilution Configuration for Preparative LC-MS", K. Blom, J. Combi. Chem., 2002, 4, 295-301; Blom et al, "Optimizing Preparative LC-MS Configurations and Methods for Parallel Synthesis Purification", J. Combi. Chem., 2003, 5, 670-83; and Blom *et al.*, "Preparative LC-MS Purification: Improved Compound Specific Method Optimization", J. Combi. Chem., 2004, 6, 874-883.

The compounds described herein can be obtained from commercial sources or synthesized by conventional methods as shown below using commercially available starting materials and reagents. The following abbreviations have been used in the examples:

EA: Ethyl Acetate;

STAB: Sodium triacetoxyborohydride;

TBAI: Tetrabutylammonium Iodide;

DMF: Dimethylformamide;

THF: Tetrahydrofuran;

TEA: Triethylamine;

TLC: Preparative thin layer chromatography;

AcOH or HOAC: Ethanoic acid;

BSA: Bovine serum album;

DCM: Dichloromethane;

DDQ: 2,3-Dichloro-5,6-dicyano-p-benzoquinone;

DMSO: Dimethyl sulfoxide;

EtOAc: Ethyl acetate;

h or hrs: hour or hours;

HTRF: Homogeneous Time Resolved Fluorescence;

MeOH: Methanol;

min: minute;

PE: petroleum ether;

Pd (dppf)Cl_2: [1,1′-Bis(diphenylphosphino)ferrocene]dichloropalladium;

rt or RT: room temperature;

TBAI: Tetrabutylammonium Iodide;

THF: Tetrahydrofuran;

$Pd_2(dba)_3$: Tris(dibenzylideneacetone)dipalladium;

NBS: N-Bromosuccinimide

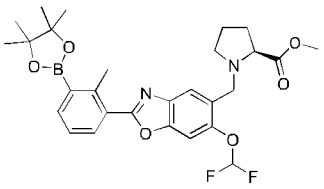
BPO: Benzoyl peroxide

TLC: Preparative thin layer chromatography.

Syntheses of Intermediates

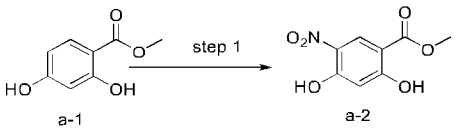
Example A synthesis of Intermediate A

methyl ((6-(difluoromethoxy)-2-(2-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzo[d]oxazol-5-yl)methyl)-L-prolinate



intermediate A

Step 1: Preparation of methyl 2,4-dihydroxy-5-nitrobenzoate

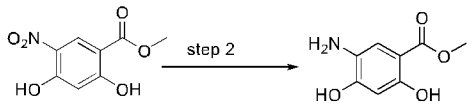


a-1 a-2

Methyl 2,4-dihydroxybenzoate (850 g) was dissolved in a mixture of glacial AcOH (3.6 L) and Ac_2O (900 mL). After cooling the clear solution to 10 °C (ice bath), a mixture of concentrated HNO_3 (65%) (455ml) in glacial AcOH (500 mL) was added over 1 h. The light brown solution was allowed to rise to 15-20 °C and stirring was continued for a further 1h. The

reaction solution was poured into H_2O (3 L). The precipitate was filtered and rinsed with small amounts of H_2O. Then pour the crude product into MeOH (2 L) with stirring. The precipitate was filtered, rinsed with small amounts of MeOH, dried under vacuum to get the tilte product 480 g.

Step 2: Preparation of methyl 5-amino-2,4-dihydroxybenzoate



a-2 a-3

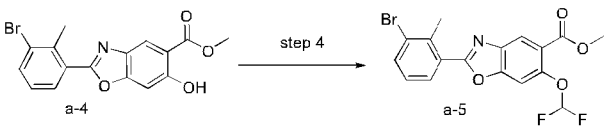
A mixture of compound a-2 (77.1 g) and 10% Pd(OH)/C (11.5 g) in methanol (2 L) was stirred under 1.1 atm of hydrogen pressure at room temperature for 3 hrs. The catalyst was then removed by filtration, the solid residue was washed with methanol (300 mL) and the solvent was removed in vacuo. This resulted in 72 g methyl 5-amino-2,4-dihydroxybenzoate.

Step 3: Preparation of methyl 2-(3-bromo-2-methylphenyl)-6-hydroxybenzo[d]oxazole-5-carboxylate

a-3 a-4

A mixture of methyl 5-amino-2,4-dihydroxybenzoate (32.9 g) and 3-bromo-2-methylbenzaldehyde (32.5 g) in MeOH (1 L) was stirred for 2.5 hrs at 80 °C， Then the resulting mixture was concentered under reduced pressure. The mixture was added DCM (500 ml), and DDQ (55.6 g) was added. The mixture was stirred at room temperature for 1 h. The reaction was diluted with DCM and washed with aqueous $Na_2S_2O_3$ solution and $NaHCO_3$ solution. The organic phases were dried over $MgSO_4$, filtered and the filtrate was concentrated. The crude product was purified by column chromatography (PE: DCM = 1/1) to afford 45 g methyl 2-(3-bromo-2-methylphenyl)-6-hydroxybenzo[d]oxazole-5-carboxylate as a brown solid.

Step 4: Preparation of methyl 2-(3-bromo-2-methylphenyl)-6-(difluoromethoxy)benzo[d]oxazole-5-carboxylate

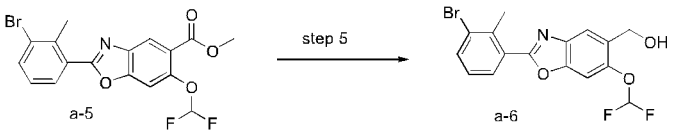


a-4 a-5

Methyl 2-(3-bromo-2-methylphenyl)-6-hydroxybenzo[d]oxazole-5-carboxylate (10.0g), sodium 2-bromo-2,2-difluoroacetate(5.46g), Cs_2CO_3(27.09g), KI(4.59g), TBAI(10.22g) was added into DMF(200mL) , The mixture was stirred at 100°C for 3 hrs. The reaction was diluted with DCM and washed with saturated NaCl solution. The crude product was purified by column

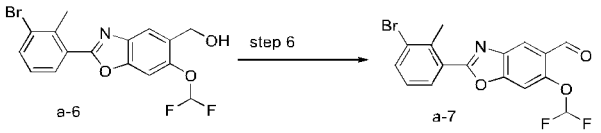
chromatography (PE: DCM=1/1) to afford 5g methyl 2-(3-bromo-2-methylphenyl)-6-(difluoromethoxy)benzo[d]oxazole-5-carboxylate.

Step 5: Preparation of (2-(3-bromo-2-methylphenyl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl) methanol



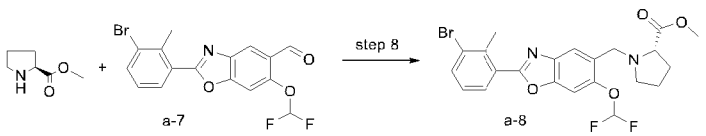
To a solution of methyl 2-(3-bromo-2-methylphenyl)-6-(difluoromethoxy) benzo[d]oxazole-5-carboxylate (1.30 g)in THF (50 mL) was added $LiAlH_4$ in THF (2.5 M) dropwise at -10 °C. The mixture was warmed up to room temperature. After 1 h, the mixture was quenched with 1 mL H_2O and 1 mL 10% NaOH solution, washed with 1 M HCl, water and brine. The organic layers were dried over Na_2SO_4, filtered and the filtrate was concentrated. This resulted (2-(3-bromo-2-methylphenyl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl) methanol as a yellow solid (1.2 g).

Step 6: Preparation of 2-(3-bromo-2-methylphenyl)-6-(difluoromethoxy) benzo[d]oxazole-5-carbaldehyde



To a solution of (2-(3-bromo-2-methylphenyl)-6-(difluoromethoxy) benzo [d]oxazol-5-yl) methanol (1.40 g) in dry THF (15 mL) was added Dess-Martin (2.39 g) in portions at 10 °C. The resulting solution was stirred for 1 h at room temperature. The mixture was filtered through celite. The solids were washed with DCM, and the combined filtrates were washed with sodium bicarbonate aqueous solution, water and brine, dried and concentrated. The residue was purified by column chromatography (eluting with hexane-EtOAc using a gradient from 20:1 to 5:1) to afford 2-(3-bromo-2-methylphenyl)-6-(difluoromethoxy) benzo[d]oxazole-5-carbaldehyde (1.27 g).

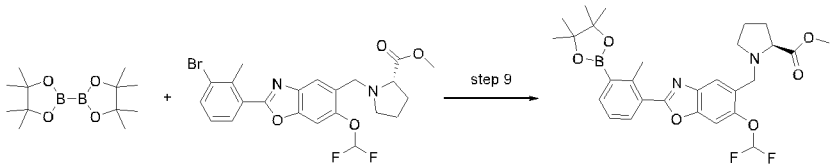
Step 7: Preparation of methyl ((2-(3-bromo-2-methylphenyl)-6-(difluoromethoxy) benzo[d]oxazol-5-yl)methyl)-L-prolinate



A solution of 2-(3-bromo-2-methylphenyl)-6-(difluoromethoxy) benzo[d]oxazole-5-carbaldehyde (1.0 g), methyl L-proline (1.7 g), HOAC (316 mg) in MeOH was stirred at room

temperature for 30 mins. The mixture was added $NaBH_3CN$ (498 mg), then was heated at 60 °C for 2 hrs. The mixture was cooled, diluted with DCM and washed with H_2O and NaCl solution. The organic phases were dried over $MgSO_4$, filtered and the filtrate was concentrated. The residue was purified by column chromatography (DCM : MeOH = 10:1), to afford 671 mg methyl ((2-(3-bromo-2-methylphenyl)-6-(difluoromethoxy) benzo[d]oxazol-5-yl)methyl)-L-prolinate as a white solid.

Step 8: Preparation of methyl ((6-(difluoromethoxy)-2-(2-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzo[d]oxazol-5-yl)methyl)-L-prolinate

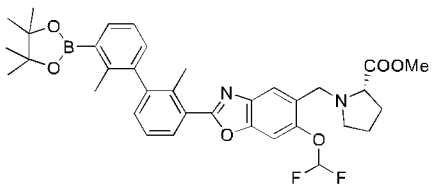


a-8 intermediate A

To a solution of methyl ((2-(3-bromo-2-methylphenyl)-6-(difluoromethoxy) benzo[d] oxazol-5-yl)methyl)-L-prolinate (680 mg) in 1,4-dioxane (16.0 ml) was added Bis(pinacolato)diboron (1.20 g), $Pd(dppf)Cl_2$·DCM (100 mg), and KOAc (102 mg) under N_2 protection. The reaction mixture was heated at 100 °C for 10 hrs. It was diluted with 30 mL of water and then extracted with DCM (90 ml×2). The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was was purified by silicagel (eluting with hexane-EtOAc using a gradient from 4:1 to 2:1) to afford methyl ((6-(difluoromethoxy)-2-(2-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzo[d]oxazol-5-yl)methyl)-L-prolinate (500 mg) . LC-MS(m/z):543.2$(M+H)^+$.

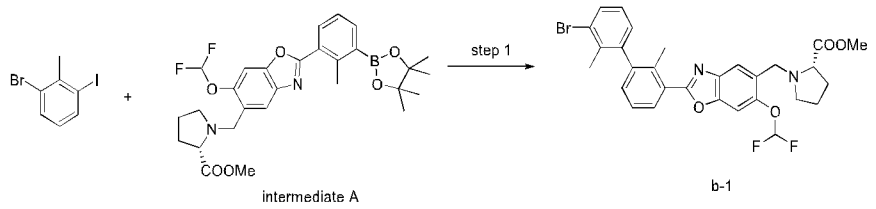
Example B synthesis of Intermediate B

methyl ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-prolinate



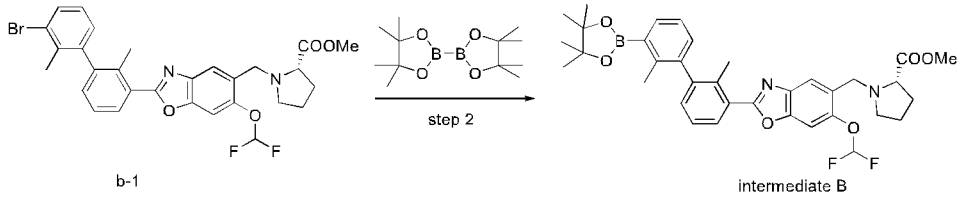
intermediate B

Step 1: Preparation of methyl ((2-(3'-bromo-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-prolinate



To a solution of intermediate A (21.7 g), 1-bromo-3-iodo-2-methylbenzene (9.0 g) in toluene (150 mL), EtOH (30 mL), 10% Na_2CO_3 aq. (30 mL), Pd(dppf)Cl_2.DCM (1.0 g) was added under N_2 protection. The mixture was allowed to stir at 90 °C overnight. The reaction was quenched with H_2O (100 mL) and extracted with EtOAc (100 mL) for 3 times. The organic layers were combined and washed with brine. The resulting solution was concentrated and purified by silicagel (eluting with Hexane-EtOAc using a gradient from 10:1 to 4:1) to afford methyl ((2-(3'-bromo-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-prolinate (18.2 g) as a brown oil.

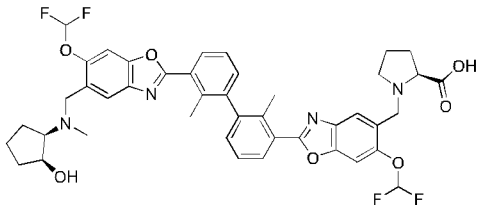
Step 2: Preparation of methyl ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-prolinate



To a solution of compound b-1 (18.2 g) in 1,4-dioxane (120 mL) was added Bis(pinacolato)diboron (12.4 g), Pd(dppf)Cl_2.DCM (1.0 g) and KOAc (9.9 g) under N_2 protection. The reaction mixture was heated at 100 °C for 6 hrs. It was diluted with 300 mL of water and then extracted with EtOAc (150 ml) for three times. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was was purified by silicagel (eluting with hexane-EtOAc using a gradient from 20:1 to 10:1) to afford methyl ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-prolinate (15.1 g) as a brown oil. LC-MS(m/z):633.9$(M+H)^+$.

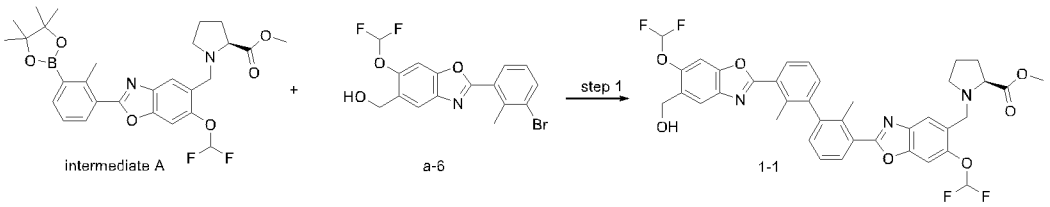
Example 1 Synthesis of Compound 1

((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((((1R,2S)-2-hydroxycyclopentyl)(methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline



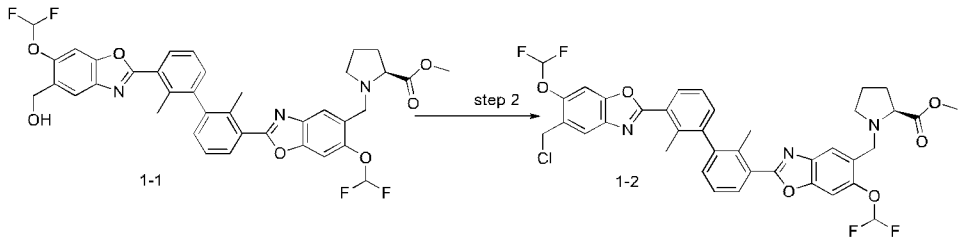
Compound 1

Step 1: Preparation of methyl ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(hydroxymethyl)benzo [d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-prolinate



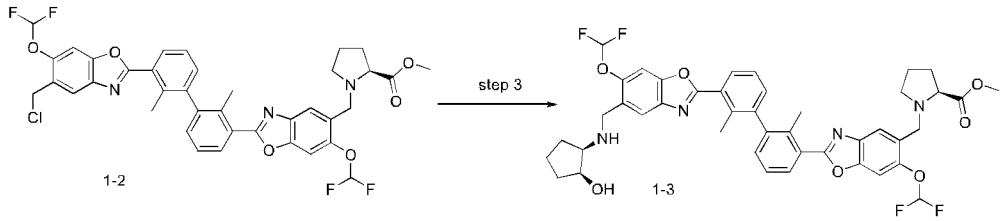
To a mixture of intermediate A (5 g) in 1,4-dioxane(80mL) /H_2O (16 mL) was added compound a-6 (3.9 g), K_2CO_3 (3.8 g) and Pd(dppf)$Cl_2CH_2Cl_2$ (732 mg). The mixture was stirred at 80 °C for 12 hrs under N_2 atomsphere. Until the raw material is almost finished and the reaction stoped, the mixture was poured into H_2O (300 mL) and extracted with DCM (100 mL) for 3 times. The organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, concentrated to get a residue. The residue was further purified by Silica gel column to get the compound 1-1(3.7g).

Step 2: Preparation of methyl ((2-(3'-(5-(chloromethyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy) benzo[d] oxazol-5-yl) methyl)-L-prolinate



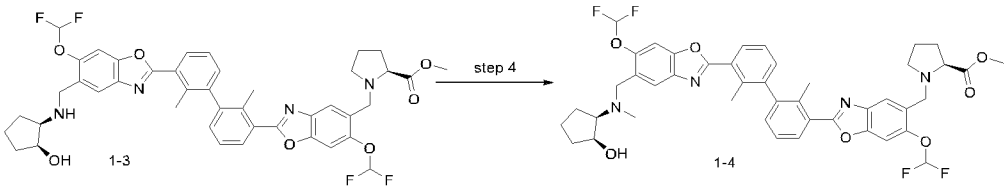
Compound 1-1 (1.5 g) was dissolved in DCM (20 mL). $SOCl_2$ (495 mg) was added dropwises and stirred at room temperature for 1 h. Until the raw material was vanished and the reaction stops, the resulting mixture was concentered under reduced pressure. This resulted in 1.56 g compound 1-2(crude).

Step 3: Preparation of methyl ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((((1R,2S)-2-hydroxycyclopentyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-prolinate



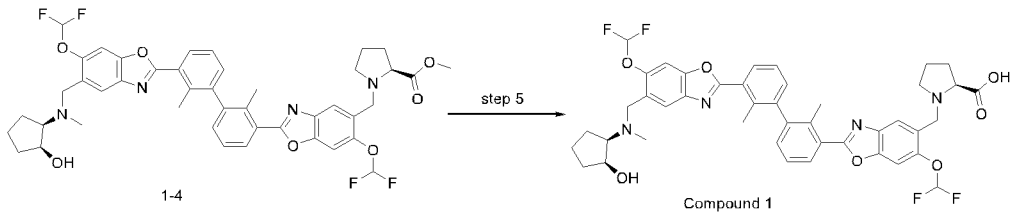
A mixture of compound 1-2(300 mg), (1S, 2R)-2-aminocyclopentan-1-ol (168 mg) , K_2CO_3 (283 mg), KI (68 mg) in CH_3CN (10 mL) was stirred at 50 °C for 1.5 hrs. Until the raw material was almost finished and the reaction stops, the reaction solution was poured into H_2O (30 mL) and extracted with DCM (15 mL) for 3 times. The organic layers were washed with brined, dried over anhydrous Na_2SO_4, filered and concentrated under reduced pressure to get the crude product. The crude product was further purified by Silica gel column (DCM/MeOH) to get compound 1-3 (240 mg).

Step 4: Preparation of methyl ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((((1R,2S)-2-hydroxycyclopentyl)(methyl) amino)methyl) benzo[d]oxazol-2-yl)-2,2'-dimethyl -[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-prolinate



A mixture of compound 1-3 (240 mg), HCHO (45 mg), CH_3COOH (36 mg) in MeOH (5 mL)/DCM (5 mL) was stirred at 30 °C for 30 mins, then $NaBH_3CN$ (57 mg) was added and continue stirred, until the raw material was almost finished and the reaction stopps. The reaction solution was poured into H_2O (30 mL) and extracted with DCM (15 mL) for 3 times. The organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to get the crude product. The crude product was further purified by Silica gel column (DCM/MeOH) to get compound 1-4 (200 mg).

Step 5: Preparation of ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((((1R,2S)-2-hydroxycyclopentyl)(methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline(compound 1)

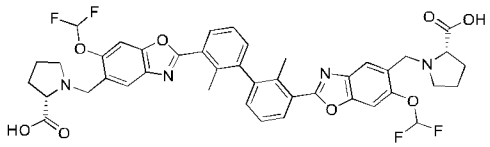


1-4 Compound 1

Compound 1-4 (200 mg) and LiOH (51 mg) was dissolved in a mixture of THF (8 mL) / H_2O (2 mL) and stirred at 35 °C for 12 hrs. The reaction solution was poured into H_2O (30 mL) and extracted with DCM (10 mL)/MeOH (5 mL) for 3 times. The organic layers were combined, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. This resulted in 160mg ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((((1R,2S)-2-hydroxycyclopentyl)(methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline (compound 1).LC-MS(m/z):803.3$(M+H)^+$.

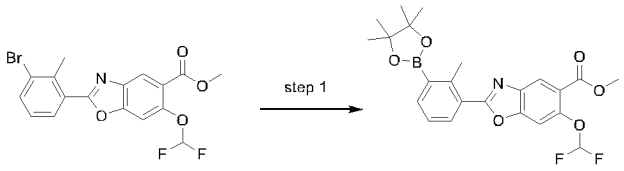
Example 2 Synthesis of Compound 2

(2'S)-(((2,2'-dimethyl-[1,1'-biphenyl]-3,3'-diyl)bis(6-(difluoromethoxy)benzo[d]oxazole-2,5-diyl))bis(methylene))di-L-proline



Compound 2

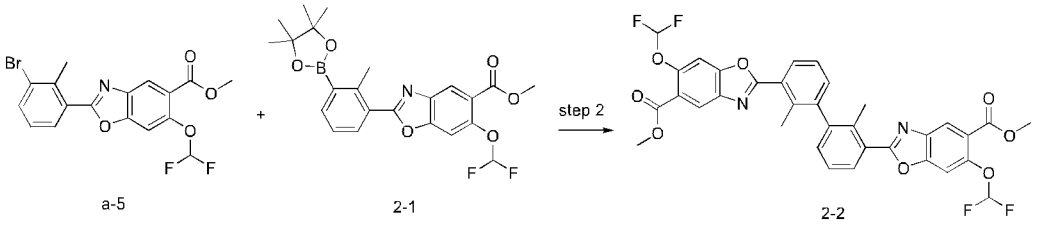
Step 1: Preparation of methyl 6-(difluoromethoxy)-2-(2-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)benzo[d]oxazole-5-carboxylate



a-5 2-1

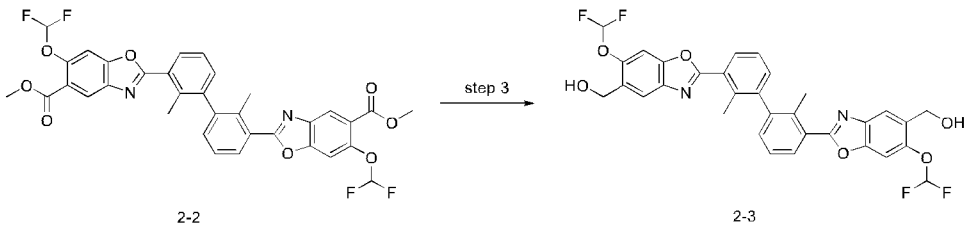
To a solution of compound a-5 (880 mg) in 1, 4-dioxane (16.0 mL) was added Bis (pinacolato) diboron (1.80 g), Pd(dppf)Cl_2·DCM (150 mg), and KOAc (130 mg). The reaction mixture was heated at 100 °C for 10 hrs. It was diluted with 30 mL water and then extracted with DCM (90 mL ×2). The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated in vacuo to get the recidue. The residue was purified by silicagel (eluting with hexane-EtOAc using a gradient from 4:1 to 2:1) to afford compound 2-1 (600 mg).

Step 2: Preparation of dimethyl2, 2'-(2, 2'-dimethyl-[1, 1'-biphenyl]-3, 3'-diyl) bis (6-(difluoromethoxy) benzo[d]oxazole-5-carboxylate)



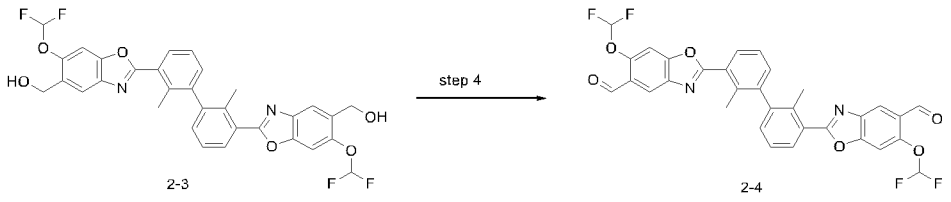
A mixture of compound 2-1 (8 g), compound a-5 (8.95 g), K_2CO_3 (5.25 g) and Pd(dppf)cl_2.DCM (1.65 g) in 1,4-Dioxane(160 mL)/H_2O (16 mL) was evacuated and refilled three times using nitrogen. The mixture was heated at reflux for 2 hrs. The reaction was added 200 mL H_2O and extracted with EtOAc (2×200 mL). The combined organic layers were washed with brine (100 mL), and then dried over Na_2SO_4. The resulting solution was filtered and concentrated to get a residue. The residue was purified by Column chromatography (EA) to get the compound 2-2 (6.3 g).

Step 3: Preparation of ((2,2'-dimethyl-[1,1'-biphenyl]-3,3'-diyl)bis(6-(difluoromethoxy) benzo[d] oxazole-2,5-diyl))dimethanol



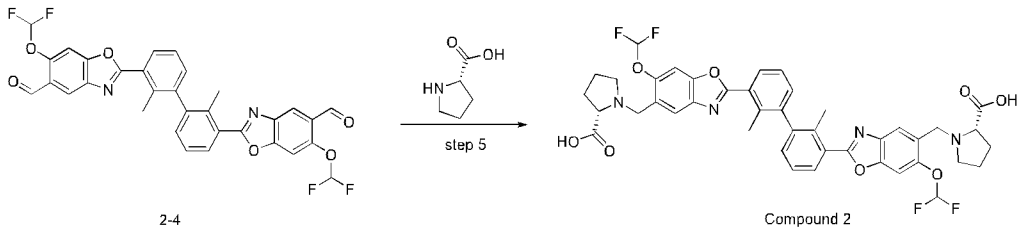
The $LiAlH_4$ (2.5M) was added dropwise to the solution of compound 2-2 (6.3 g) in THF (150 mL) at 0 °C. The mixture was stirred at 0 °C for 30 mins. The reaction mixture was quenched with H_2O at 0 °C. The mixture was dried over Na_2SO_4, filtered and concentrated to get the compound 2-3 (5.7 g).

Step 4: Preparation of 2,2'-(2,2'-dimethyl-[1,1'-biphenyl]-3,3'-diyl)bis(6-(difluoromethoxy) benzo[d]oxazole-5-carbaldehyde)



The Dess-Martin (11.95 g) was added to the solution of compound 2-3 (5.70 g) in THF (100 mL). The mixture was stirred at RT for 2hrs. The reaction was quenched with $NaHCO_3$ and Na_2SO_3 and extracted with EtOAc (2×100 mL). The combined organic layers were washed with brine (100 mL), dried over Na_2SO_4, filtered and concentrated to get the compound 2-4 (5.5 g).

Step 5: Preparation of (2'S)-(((2,2'-dimethyl-[1,1'-biphenyl]-3,3'-diyl)bis(6-(difluoromethoxy)benzo[d]oxazole-2,5-diyl))bis(methylene))di-L-proline(compound 2)

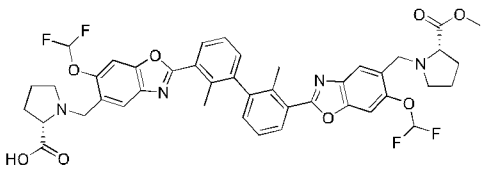


2-4 Compound 2

A mixture of compound 2-4 (4 g), L-proline (4.58 g) and AcOH (0.82 g) in MeOH (100 mL) was stirred for 30 mins. $NaBH_3CN$ was added to the mixture and the mixture was stirred for 12 hrs. The reaction was added 200 mL H_2O and extracted with DCM (2×200 mL). The combined organic layers were dried over Na_2SO_4. The resulting solution was filtered and concentrated to get the crude product. The crude product was purified by Column chromatography (DCM/MeOH = 10:1) to get 2.56 g (2'S)-(((2,2'-dimethyl-[1,1'-biphenyl]-3,3'-diyl)bis(6-(difluoromethoxy)benzo[d]oxazole-2,5-diyl))bis(methylene))di-L-proline (compound 2). LC-MS(m/z):803.3$(M+H)^+$.

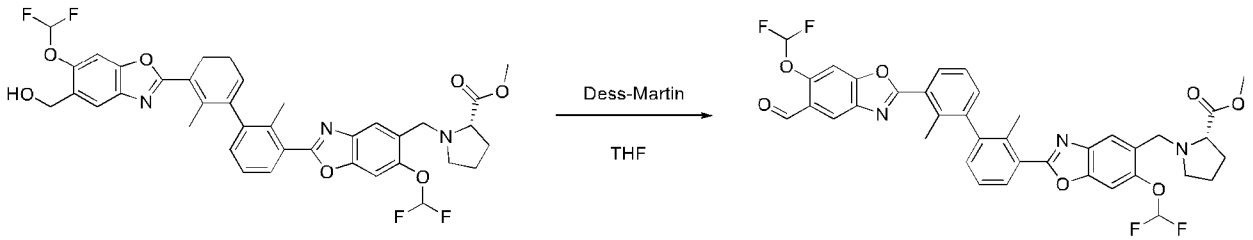
Example 3 Synthesis of Compound 3

((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((S)-2-(methoxycarbonyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline



Compound 3

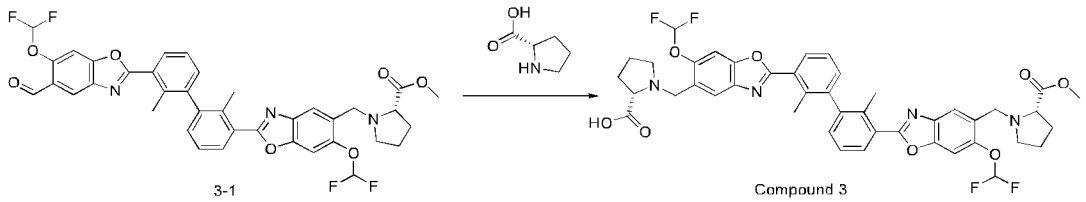
Step 1 Preparation of methyl ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-formylbenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-prolinate



1-1 3-1

The Dess-Martin(11.79g) was added to the solution of compound 1-1(10.00g) in THF (200ml) in portions. The mixture was stirred for 2h at RT. The reaction was quenched with Na_2SO_3 and sodium bicarbonate aqueous solution. The Reaction was extracted with EtOAc (2×150ml). The combined organic phase was washed with brine(100ml), dried over Na_2SO_4, filtered and concentrated to get the compound 3-1(9.50g).

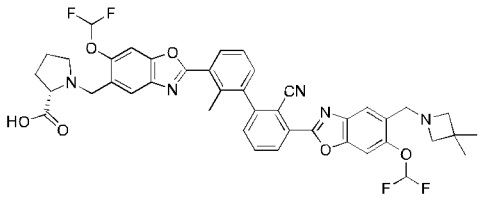
Step 2: Preparation of ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((S)-2-(methoxycarbonyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline



A mixture of compound 3-1 (5.90 g), L-proline (2.85 g) and AcOH (0.51 g) in MeOH (60 mL) was stirred for 30 mins. Then $NaBH_3CN$ (1.55g) was added to the mixture. The reaction was stirred for 3 hrs. The reaction was added 100 mL H_2O and extracted with DCM (2×100 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated to get the residue. The residue was purified by Column chromatography (DCM/MeOH = 10:1) to get ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((S)-2-(methoxycarbonyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline (3.6 g). LC-MS(m/z):817.3$(M+H)^+$.

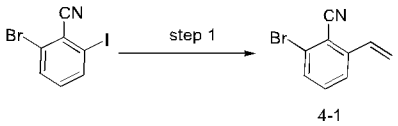
Example 4 Synthesis of Compound 4

((2-(2'-cyano-3'-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline



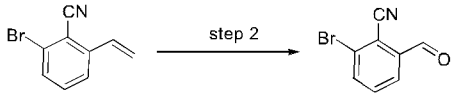
Compound 4

Step 1: Preparation of 2-bromo-6-vinylbenzonitrile



A mixture of 2-bromo-6-iodobenzonitrile (10g), 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (5g), [1,1′ -Bis(diphenylphosphino)ferrocene]dichloropalladium(II) (2.5g), and Potassium carbonate (13.4g) in 1,4-dioxane (100 mL)/H_2O (20 mL) was stirred at 80°C for 12hrs under N_2 atmosphere. The reaction solution was poured into H_2O (30mL) and extracted with DCM (15mL×3). The organic layers were washed with brine, dried overanhydrous Na_2SO_4, filtered and concentrated under reduced pressure to get the crude product. The crude product was further purified by Silica gel column to get the compound 4-1 (5g).

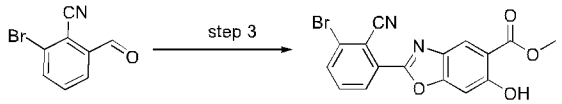
Step 2: Preparation of 2-bromo-6-formylbenzonitrile



4-1 4-2

A mixture of compound 4-1 (1g) and sodium periodate(3.67g) in THF (20 mL)/H_2O (6 mL)was stirred under ice bath, then potassium osmate(20mg) was added and the mixture was stirred at room temperature for 4 hrs. The reaction mixture was poured into H_2O (150mL) and extracted with EA(100mL) for 2 times, the organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated to get the title compound 4-2 (800mg).

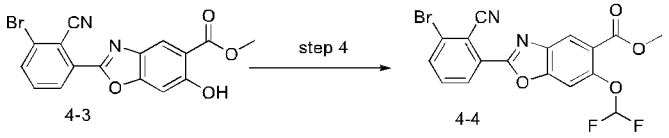
Step 3: Preparation of methyl 2-(3-bromo-2-cyanophenyl)-6-hydroxybenzo[d]oxazole-5-carboxylate



4-2 4-3

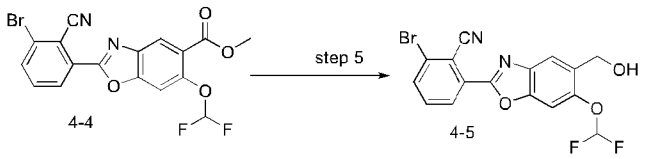
A mixture of compound4-2 (1g) and methyl 5-amino-2,4-dihydroxybenzoate(870mg) in MeOH(150mL) was stirred at 80°C for 2.5 hrs， then the reaction mixture was concentered under reduced pressure and dissolved in dichloromethane. 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (1.3g) was added into the solution and continue stirred at room temperature. After 1 h, the mixture was filtered, the filter cake was washed with dichloromethane and the filtrate was concentrate under reduced pressure to get the crude product. The crude product was suspended in methanol, the solution was filtered, and the filter cake was dried in a vacuum oven to get the title compound (1.4g).

Step 4: Preparation of methyl 2-(3-bromo-2-cyanophenyl)-6-(difluoromethoxy)benzo[d]oxazole-5-carboxylate



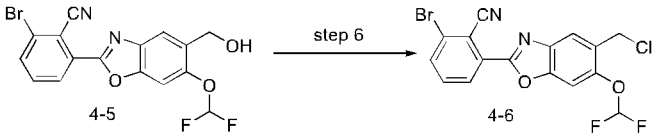
Sodium chlorodifluoroacetate(850mg), Cesium carbonate(2.62g) was added into a stirred solution of Methyl 2-(3-bromo-2-cyanophenyl)-6-hydroxybenzo[d]oxazole-5-carboxylate(1g) in DMF (20 mL)/H_2O(0.6 mL), the reaction mixture was heated to 80°C and stirred for 4 hrs. Then the mixture was poured into H_2O (100mL) and extracted with EA (80mL) for 2 times. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated to get the crude product. The crude product was further purified by Silica gel column to get the title compound 4-4 (800mg).

Step 5: Preparation of 2-bromo-6-(6-(difluoromethoxy)-5-(hydroxymethyl)benzo[d]oxazol-2-yl)benzonitrile



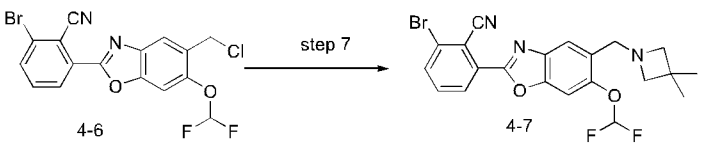
This compound was prepared using similar procedures as described as step5 in example A, with compound 4-4 replacing compound a-4. The mixture was concentrated under reduced pressure to get the title compound 4-5.

Step 6: Preparation of 2-bromo-6-(5-(chloromethyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)benzonitrile



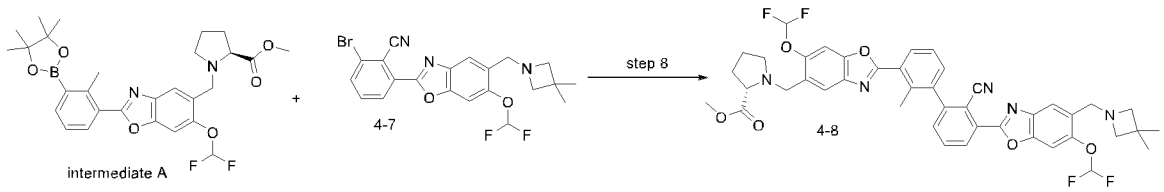
This compound was prepared using similar procedures as described as step2 in example 1, with compound 4-5 replacing compound 1-1. The crude product was used directly in the next step.

Step 7: Preparation of 2-bromo-6-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)benzonitrile



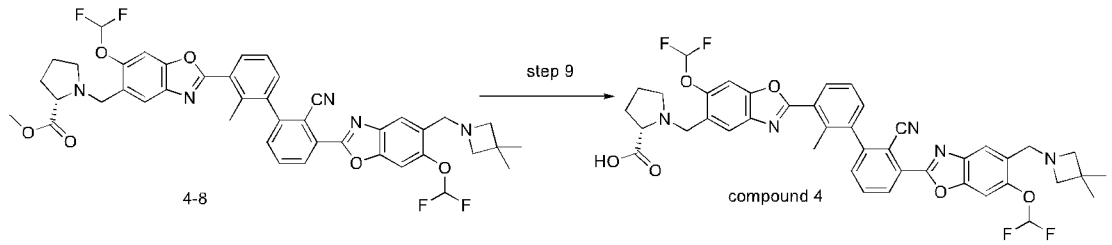
This compound was prepared using similar procedures as described as step3 in example 1, with compound 4-6 replacing compound 1-2, and with 3,3-dimethylazetidine replacing (1S, 2R)-2-aminocyclopentan-1-ol. The crude product was further purified by Silica gel column (PE/EA) to get the title compound (290mg).

Step 8: Preparation of methyl ((2-(2'-cyano-3'-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-prolinate



This compound was prepared using similar procedures as described as step1 in example 1 with compound 4-7 replacing compound a-6. The crude product was further purified by Silica gel column to get the title compound.

Step 9: Preparation of ((2-(2'-cyano-3'-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline

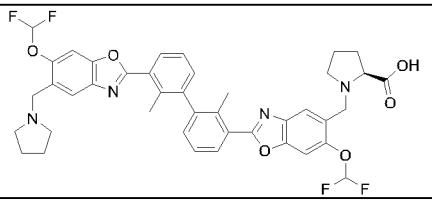
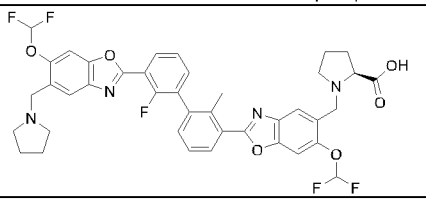
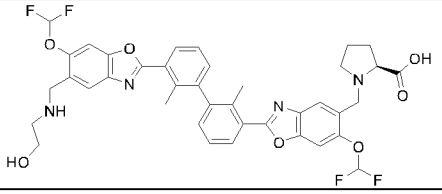
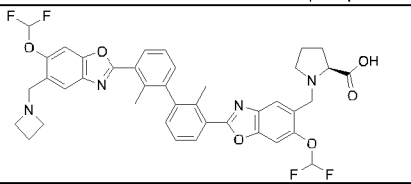
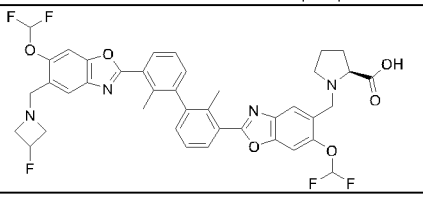
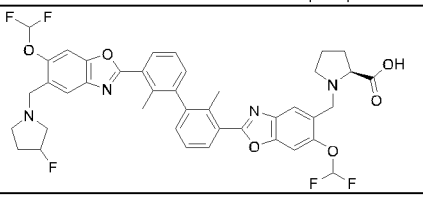
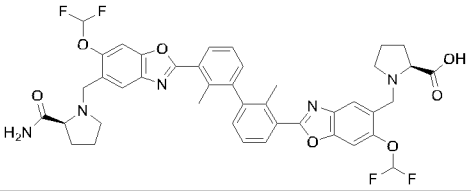
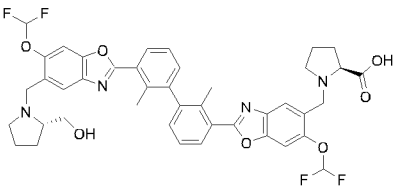
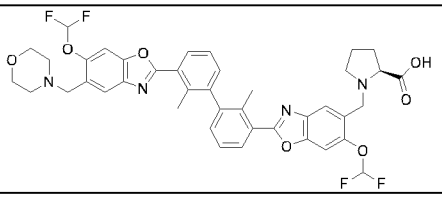
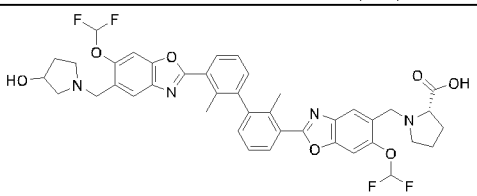


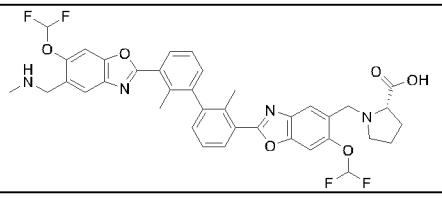
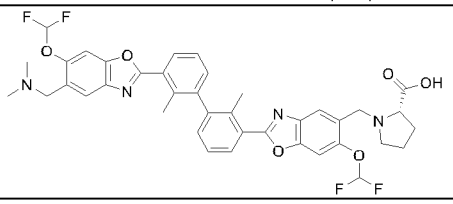
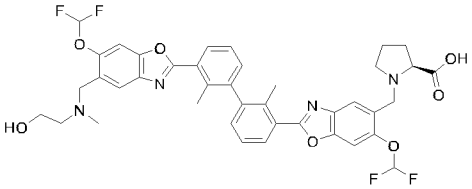
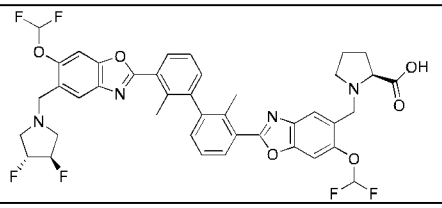
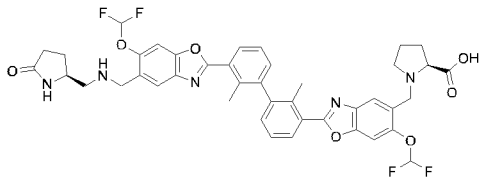
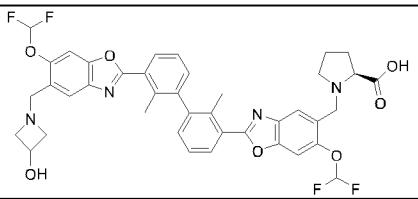
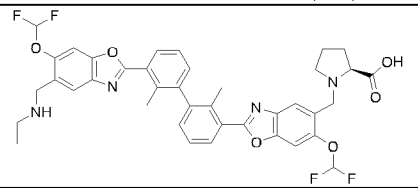
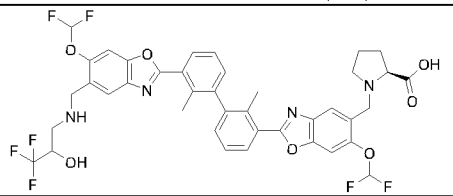
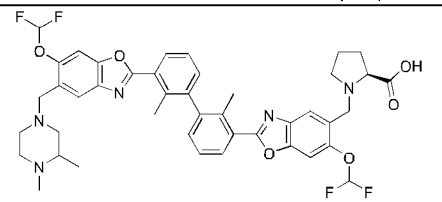
This compound was prepared using similar procedures as described as step5 in example 1, with compound 4-8 replacing compound 1-4. The mixture was concentrated under reduced pressure to get the title compound. LC-MS(m/z):784.3$(M+H)^+$.

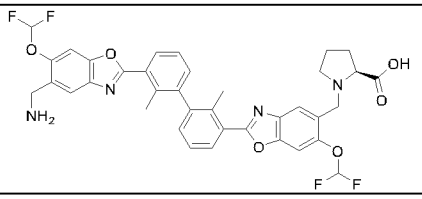
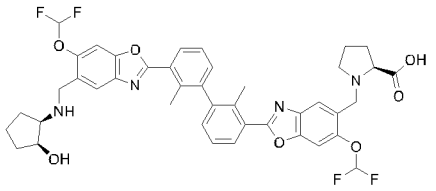
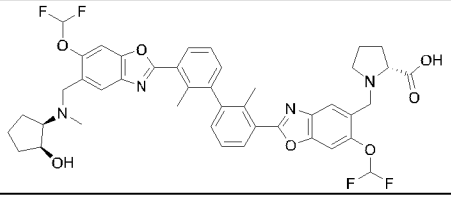
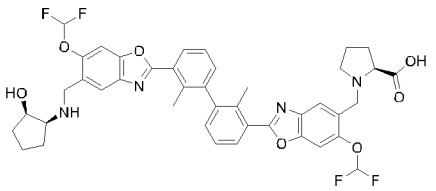
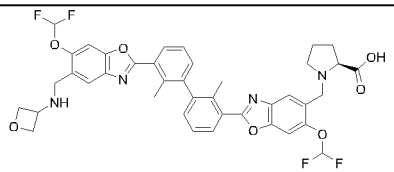
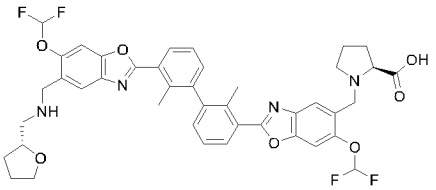
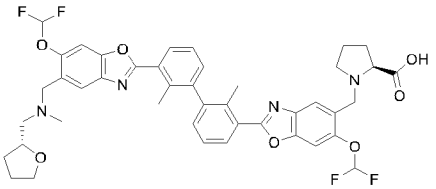
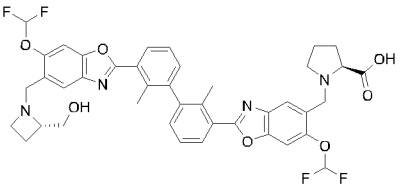
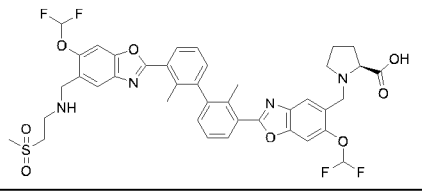
The compounds of table 1 were prepared in a similar manner to Examples 1-4 via different reaction starting materials and suitable reagents.

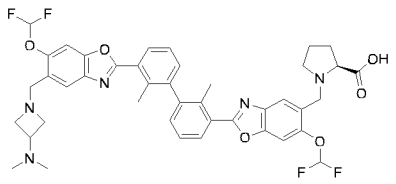
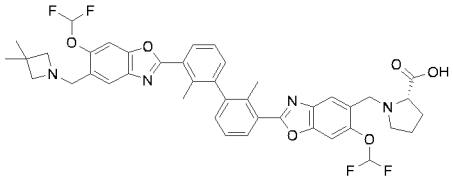
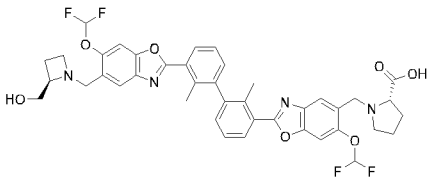
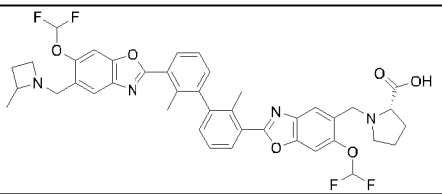
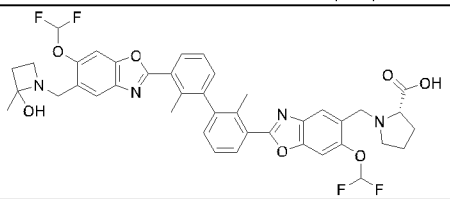
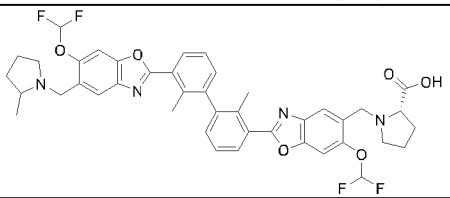
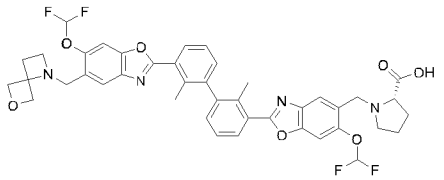
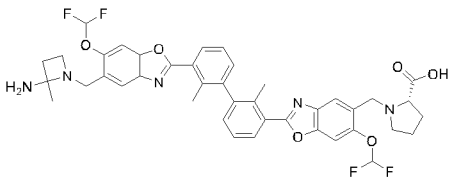
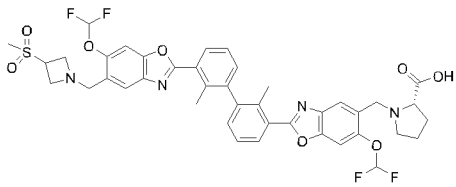
Table 1

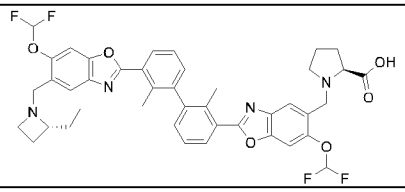
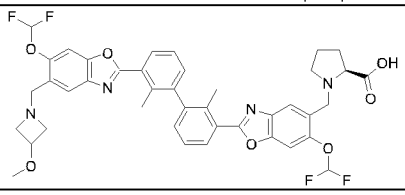
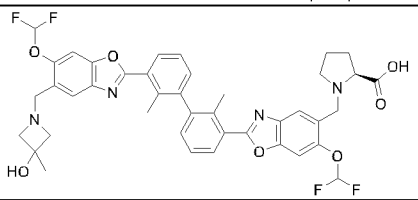
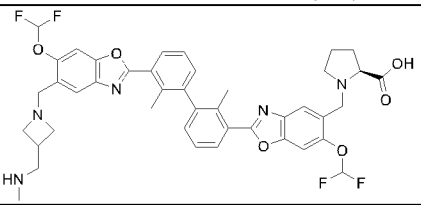
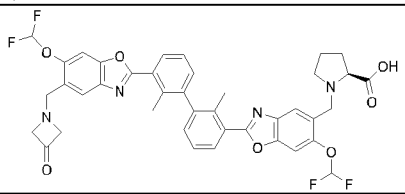
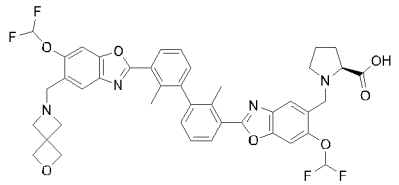
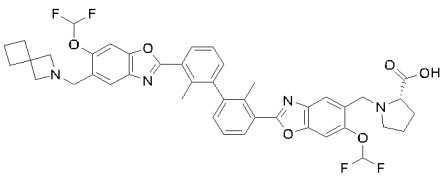
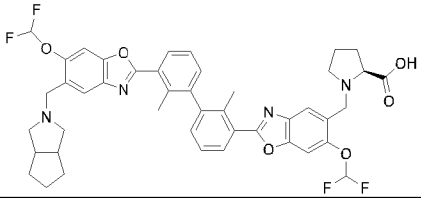
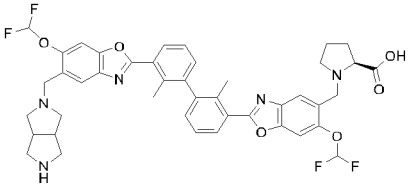
EX No.	Chemical Name	Structure	Physical Data (MS) $(M+H)^+$

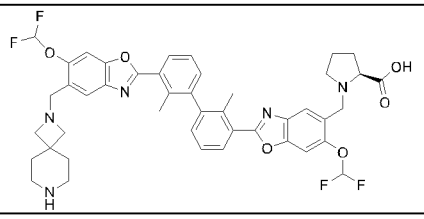
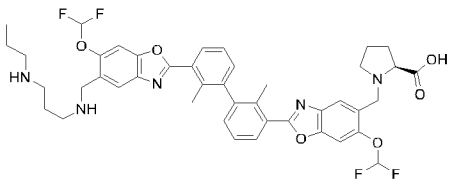
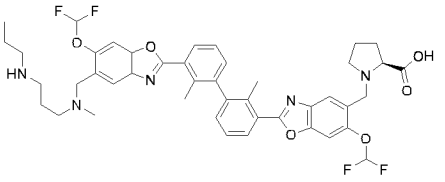
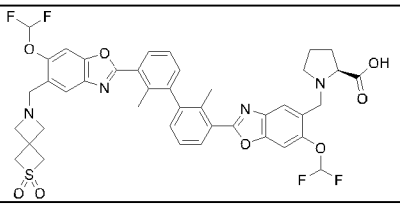
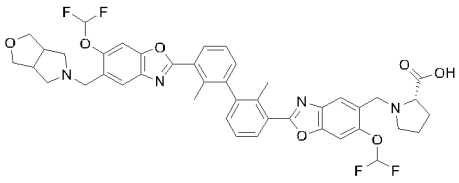
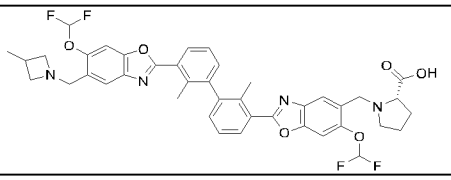
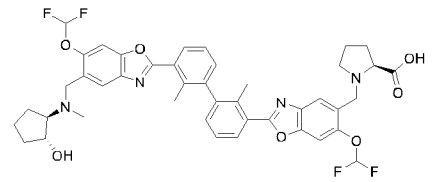
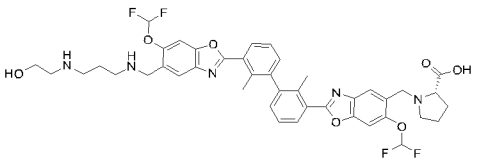
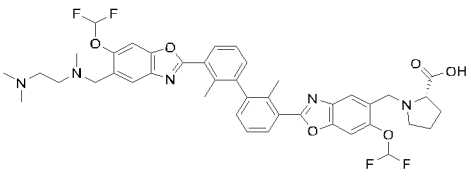
5	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		759.3
6	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2'-fluoro-2-methyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		763.3
7	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((2-hydroxyethyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		749.3
8	((2-(3'-(5-(azetidin-1-ylmethyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		744.3
9	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-fluoroazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		763.3
10	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-fluoropyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		777.3
11	((2-(3'-(5-(((S)-2-carbamoylpyrrolidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		802.3
12	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((S)-2-(hydroxymethyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		789.3
13	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(morpholinomethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		775.3
14	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-hydroxypyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		775.3

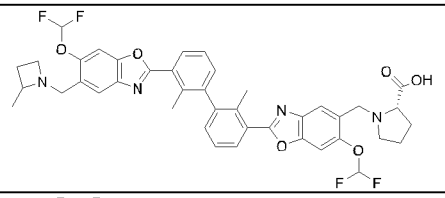
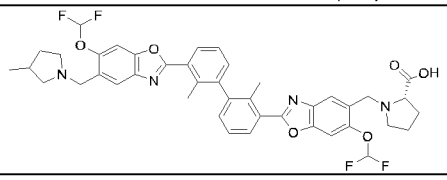
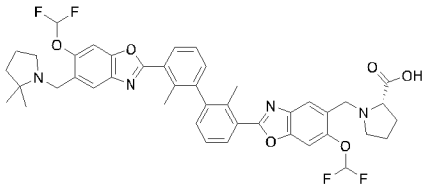
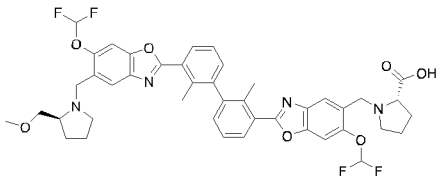
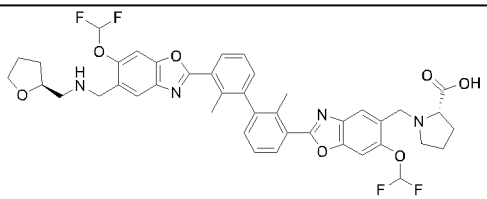
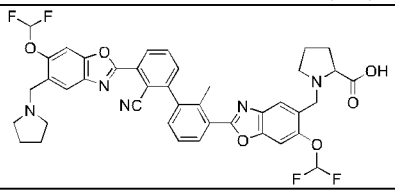
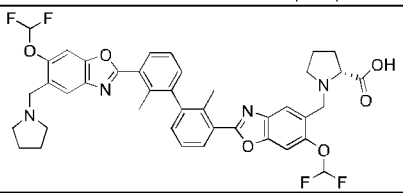
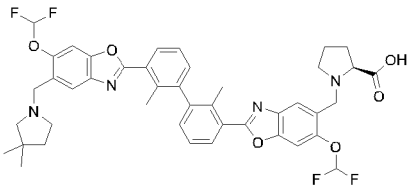
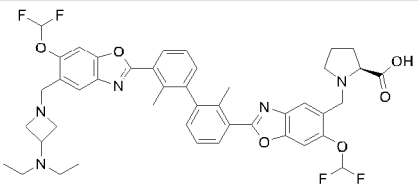
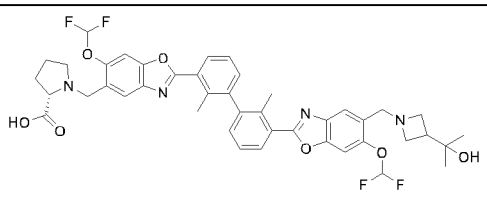
15	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((methylamino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		719.2
16	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((dimethylamino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		733.3
17	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((2-hydroxyethyl)(methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		763.3
18	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((3R,4R)-3,4-difluoropyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		795.3
19	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((((S)-5-oxopyrrolidin-2-yl)methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		802.3
20	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-hydroxyazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		761.3
21	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((ethylamino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		733.3
22	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((3,3,3-trifluoro-2-hydroxypropyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		817.2
23	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3,4-dimethylpiperazin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		802.3

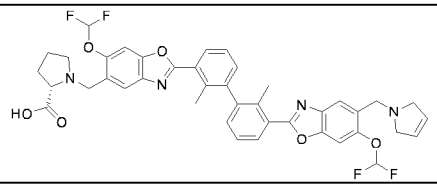
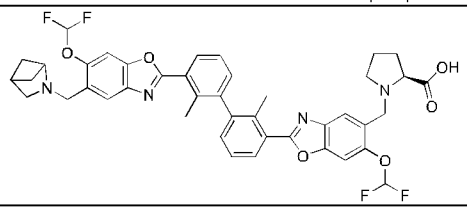
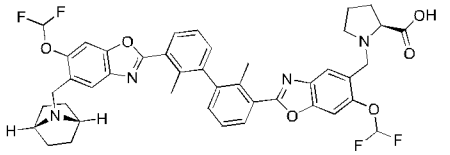
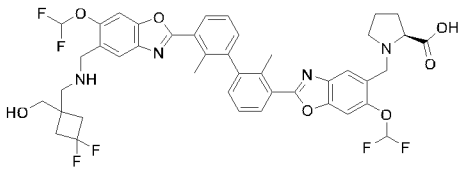
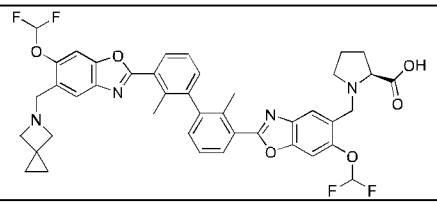
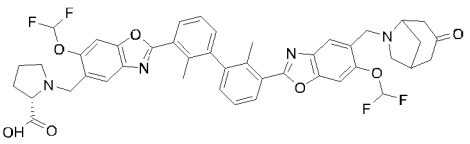
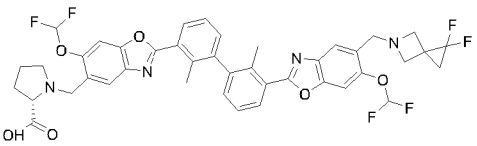
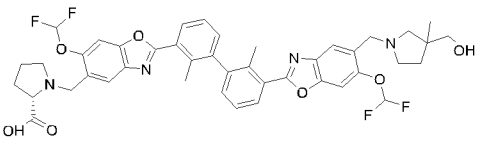
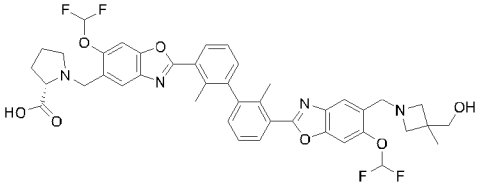
24	((2-(3'-(5-(aminomethyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		705.2
25	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((((1R,2S)-2-hydroxycyclopentyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		789.3
26	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((((1R,2S)-2-hydroxycyclopentyl)(methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-D-proline		803.3
27	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((((1S,2R)-2-hydroxycyclopentyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		789.3
28	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((oxetan-3-ylamino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		761.3
29	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((((R)-tetrahydrofuran-2-yl)methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		789.3
30	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((methyl(((R)-tetrahydrofuran-2-yl)methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		803.3
31	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((S)-2-(hydroxymethyl)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		775.3
32	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((2-(methylsulfonyl)ethyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		811.2

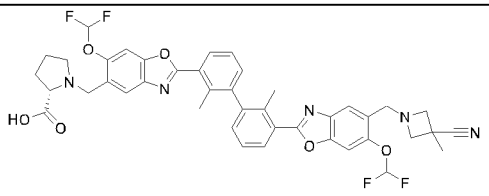
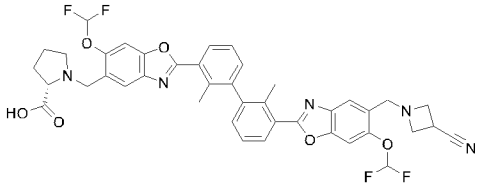
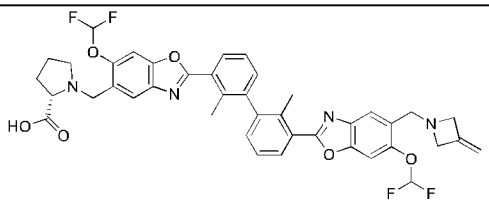
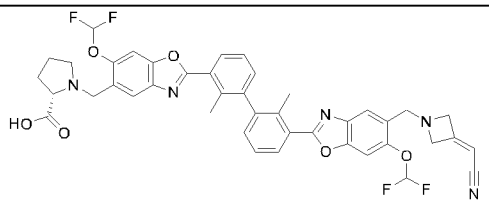
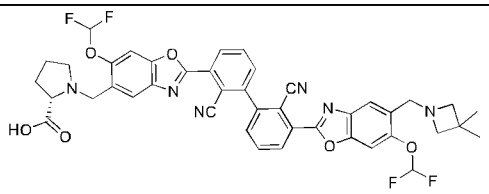
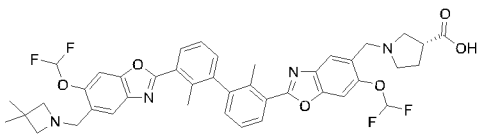
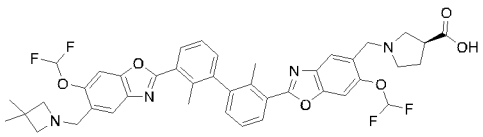
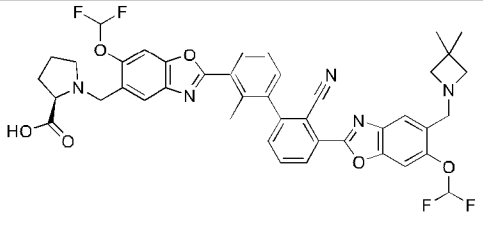
33	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-(dimethylamino)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		788.3
34	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		773.3
35	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((R)-2-(hydroxymethyl)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		775.3
36	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((2-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		759.3
37	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((2-hydroxy-2-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		775.3
38	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((2-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		773.3
39	((2-(3'-(5-((6-oxa-1-azaspiro[3.3]heptan-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		787.3
40	((2-(3'-(5-((2-amino-2-methylazetidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		774.3
41	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-(methylsulfonyl)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		823.2

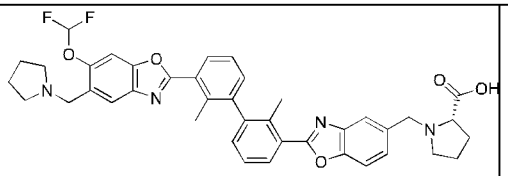
42	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((R)-2-ethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		773.3
43	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-methoxyazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		775.3
44	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-hydroxy-3-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		775.3
45	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-((methylamino)methyl)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		788.3
46	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-oxoazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		759.2
47	((2-(3'-(5-((2-oxa-6-azaspiro[3.3]heptan-6-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		787.3
48	((2-(3'-(5-((2-azaspiro[3.3]heptan-2-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		785.3
49	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((hexahydrocyclopenta[c]pyrrol-2(1H)-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		799.3
50	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		800.3

51	((2-(3'-(5-((2,7-diazaspiro[3.5]nonan-2-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		814.3
52	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((3-(propylamino)propyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		804.3
53	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((methyl(3-(propylamino)propyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		818.4
54	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((2,2-dioxido-2-thia-6-azaspiro[3.3]heptan-6-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		835.2
55	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((tetrahydro-1H-furo[3,4-c]pyrrol-5(3H)-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		801.3
56	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		759.3
57	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((((1R,2R)-2-hydroxycyclopentyl)(methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		803.3
58	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((3-((2-hydroxyethyl)amino)propyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		806.3
59	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((2-(dimethylamino)ethyl)(methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		790.3

60	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((2-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		759.3
61	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		773.3
62	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((2,2-dimethylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		787.3
63	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((S)-2-(methoxymethyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		803.3
64	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((((S)-tetrahydrofuran-2-yl)methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		789.3
65	((2-(2'-cyano-3'-(6-(difluoromethoxy)-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline		770.3
66	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-D-proline		759.3
67	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3,3-dimethylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		787.3
68	((2-(3'-(5-((3-(diethylamino)azetidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		816.3
69	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-(2-hydroxypropan-2-yl)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		803.3

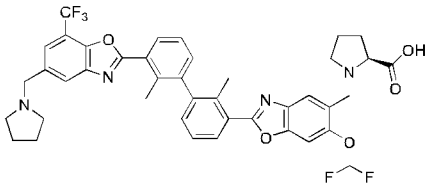
70	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((2,5-dihydro-1H-pyrrol-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		757.3
71	((2-(3'-(5-((2-azabicyclo[2.1.1]hexan-2-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		771.3
72	((2-(3'-(5-(((1s,4s)-7-azabicyclo[2.2.1]heptan-7-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		785.3
73	((2-(3'-(5-((((3,3-difluoro-1-(hydroxymethyl)cyclobutyl)methyl)amino)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		839.3
74	((2-(3'-(5-((5-azaspiro[2.3]hexan-5-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		771.3
75	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-oxo-6-azabicyclo[3.2.1]octan-6-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		813.3
76	((2-(3'-(5-((1,1-difluoro-5-azaspiro[2.3]hexan-5-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		807.3
77	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-(hydroxymethyl)-3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		803.3
78	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-(hydroxymethyl)-3-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		789.3

79	((2-(3'-(5-((3-cyano-3-methylazetidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		784.3
80	((2-(3'-(5-((3-cyanoazetidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		770.3
81	((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-methyleneazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		757.3
82	((2-(3'-(5-((3-(cyanomethylene)azetidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		782.3
83	((2-(2,2'-dicyano-3'-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		795.3
85	(R)-1-((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid		773.3
86	(S)-1-((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid		773.3
87	((2-(2'-cyano-3'-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline		784.3

317	((2-(3'-(6-(difluoromethoxy)-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		693.3

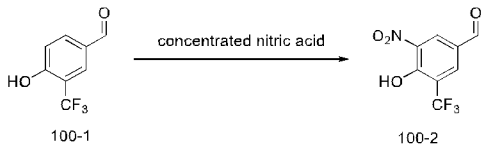
Example 100 Synthesis of Compound 100

((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline



Compound 100

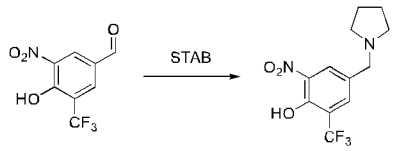
Step 1: Preparation of 4-hydroxy-3-nitro-5-(trifluoromethyl)benzaldehyde



100-1 100-2

4-hydroxy-3-(trifluoromethyl)benzaldehyde (1g) was dissolved in concentrated H_2SO_4 (10mL) . After the mixture was cooled to 5°C (ice bath), concentrated HNO_3 (65%) (612mg) was added dropwise and the mixture was stirred for another 30 mins. Until the raw material was almost finished and the reaction stopped, the mixture was poured into ice water (30 mL), isolated by filtration. This resulted in compound 100-2 (1 g).

Step 2: Preparation of 2-nitro-4-(pyrrolidin-1-ylmethyl)-6-(trifluoromethyl)phenol

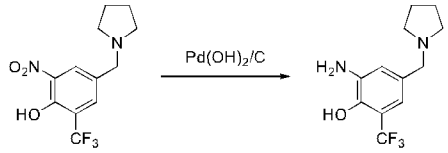


100-2 100-3

A mixture of compound 100-2 (500mg), pyrrolidine (454mg) , CH_3COOH(255mg) in 1,4-dioxane (10mL) was stirred for 30 mins at 30 °C， Then sodium triacetoxyborohydride (1.35g) was added and continue stirred. Until the raw material was almost finished and the reaction stopped, the reaction solution was poured into H_2O (30mL),extracted with DCM (15mL) for 3 times, brine and dry using anhydrous Na_2SO_4, The precipitate was filtered and dried under

vacuum, The crude product was further purified by Silica gel column (DCM / MeOH = 20:1) to get compound 100-3 (420 mg).

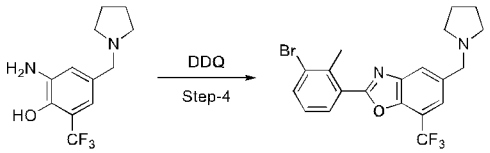
Step 3: Preparation of 2-amino-4-(pyrrolidin-1-ylmethyl)-6-(trifluoromethyl)phenol



100-3 100-4

A mixture of compound 100-3 (420 mg) and 10% Pd(OH)/C (150 mg) in methanol (10 mL) was stirred under 1.1 atm of hydrogen pressure at room temperature for 3 hrs. The catalyst was then removed by filtration, the solid residue was washed with methanol (300 mL) and the solvent was removed in vacuo. This resulted in 300 mg compound 100-4.

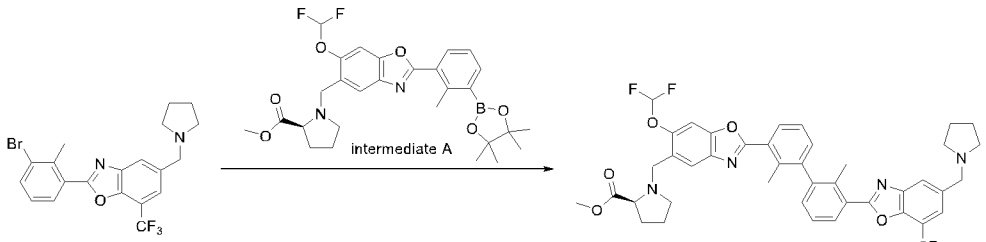
Step 4: Preparation of 2-(3-bromo-2-methyl-phenyl)-5-(pyrrolidin-1-ylmethyl)-7-(trifluoromethyl)-1,3-benzoxazole



100-4 100-5

This compound was prepared using similar procedures as described as step3 in example A, with compound 100-4 replacing compound a-3. The crude product was used directly in the next step.

Step 5: Preparation of methyl (2S)-1-[[6-(difluoromethoxy)-2-[2-methyl-3-[2-methyl-3-[5-(pyrrolidin-1-ylmethyl)-7-(trifluoromethyl)-1,3-benzoxazol-2-yl]phenyl]phenyl]-1,3-benzoxazol-5-yl]methyl]pyrrolidine-2-carboxylate

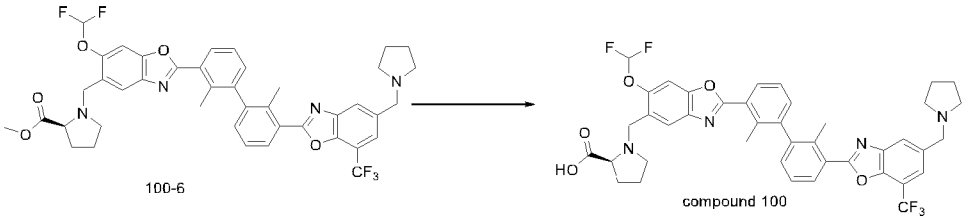


100-5 100-6

Intermediate A (345.72 mg), compound 100-5 (280 mg), 1,1'-Bis(diphenylphosphino) ferrocene palladiuM(II)dichloride (53 mg), and potassium carbonate (88.10 mg) dissolved in 1,4-dioxane (8 mL) and H_2O (2 mL) , stirred for 12 hrs at 80 °C under N_2. The reaction solution was poured into H_2O (30mL) and extracted by DCM (15mL) for 3 times. The organic

layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under vacuum to get the curde product. The crude product was further purified by Silica gel column to get the compound 100-6 (300 mg).

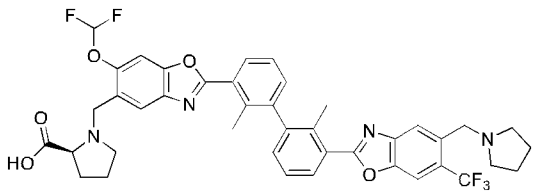
Step 6: Preparation of (2S)-1-[[6-(difluoromethoxy)-2-[2-methyl-3-[2-methyl-3-[5-(pyrrolidin-1-ylmethyl)-7-(trifluoromethyl)-1,3-benzoxazol-2-yl]phenyl]phenyl]-1,3-benzoxazol-5-yl]methyl]pyrrolidine-2-carboxylic acid (compound 100)



This compound was prepared using similar procedures as described as step5 in example 1, with compound 100-6 replacing compound 1-4. The precipitate was filtered and dried under vacuum. This resulted in (2S)-1-[[6-(difluoromethoxy)-2-[2-methyl-3-[2-methyl-3-[5-(pyrrolidin-1-ylmethyl)-7-(trifluoromethyl)-1,3-benzoxazol-2-yl]phenyl]phenyl]-1,3-benzoxazol-5-yl]methyl]pyrrolidine-2-carboxylic acid (compound 100). LC-MS(m/z):761.3$(M+H)^+$.

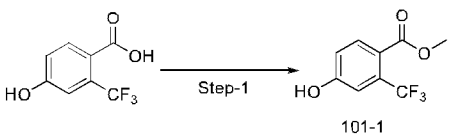
Example 101 Synthesis of Compound 101

((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)-6-(trifluoromethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline



Compound 101

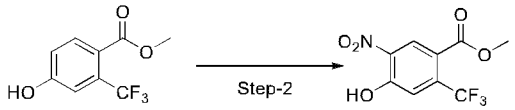
Step 1: Preparation of methyl 4-hydroxy-2-(trifluoromethyl)benzoate



To the solution of Methyl 4-hydroxy-2-(trifluoromethyl) benzoate 4-Hydroxy-2-(trifluoromethyl) benzoic acid (18.0 g) in methanol (300 ml) was added concentrated sulfuric acid (10 ml) dropwise, the mixture was stirred under reflux for 12 hrs. After cooling to room

temperature, water (200 ml) was added to the reaction mixture, methanol was distilled off under reduced pressure and the mixture was extracted twice with ethyl acetate (200 ml). The organic layer was washed with water, saturated sodium bicarbonate water and saturated aqueous sodium chloride solution, dried over sodium sulfate, filtration and concentration under reduced pressure. Title compound (18 g) was obtained.

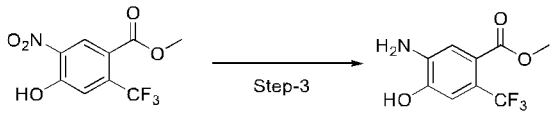
Step 2: Preparation of methyl 4-hydroxy-5-nitro-2-(trifluoromethyl)benzoate



101-1 101-2

This compound was prepared using similar procedures as described as step1 in example 100, with compound 101-1 replacing compound 100-1. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate) to get the title compound.

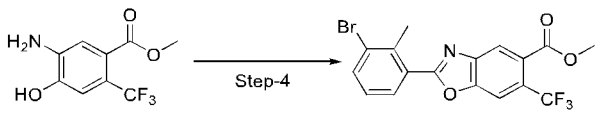
Step 3: Preparation of methyl 5-amino-4-hydroxy-2-(trifluoromethyl)benzoate



101-2 101-3

This compound was prepared using similar procedures as described as step3 in example 100, with compound 101-2 replacing compound100-3. The filtrate was concentrate under reduced pressure to get the title compound.

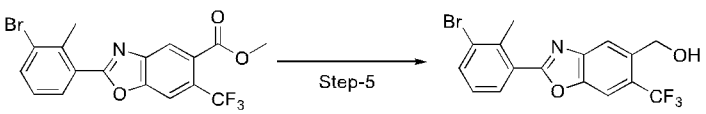
Step 4: Preparation of methyl 2-(3-bromo-2-methylphenyl)-6-(trifluoromethyl)benzo[d]oxazole-5-carboxylate



101-3 101-4

This compound was prepared using similar procedures as described as step3 in example A, with compound 101-3 replacing compound a-3. The crude product was suspended in methanol, filtered and dried in a vacuum oven. The title compound was obtained.

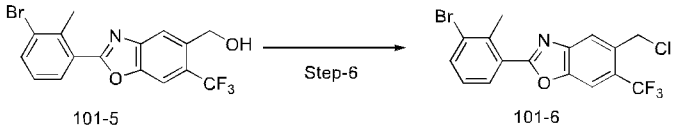
Step 5: Preparation of (2-(3-bromo-2-methylphenyl)-6-(trifluoromethyl)benzo[d]oxazol-5-yl)methanol



101-4 101-5

This compound was prepared using a similar procedure as described as step5 in example A with compound 101-4 replacing compound a-5. The filtrate was concentrate under reduced pressure and the title compound was obtained.

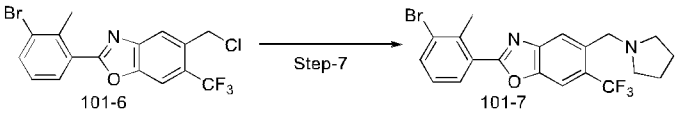
Step 6: Preparation of 2-(3-bromo-2-methylphenyl)-5-(chloromethyl)-6-(trifluoromethyl)benzo[d]oxazole



101-5 101-6

This compound was prepared using a similar procedure as described as step2 in example 1, with compound 101-5 replacing compound 1-1. The crude product was used directly in the next step.

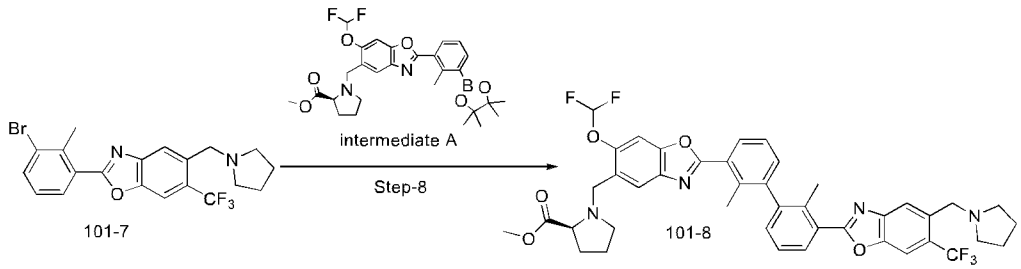
Step 7: Preparation of 2-(3-bromo-2-methylphenyl)-5-(pyrrolidin-1-ylmethyl)-6-(trifluoromethyl)benzo[d]oxazole



101-6 101-7

This compound was prepared using a similar procedure as described as step3 in example 1, with compound 101-6 replacing compound 1-2, and with pyrrolidine replacing (1S, 2R)-2-aminocyclopentan-1-ol. The crude product was further purified by Silica gel column (PE/EA) to get the title compound.

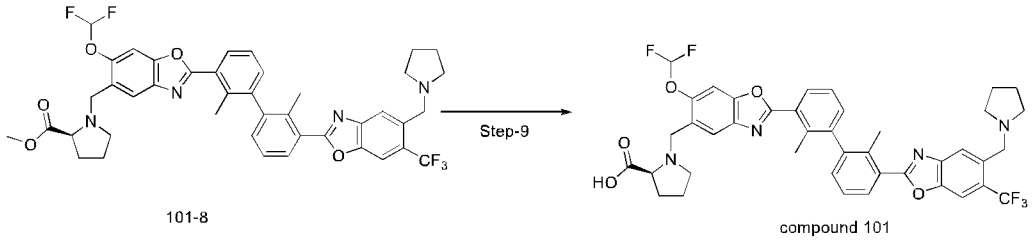
Step 8: Preparation of methyl ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)-6-(trifluoromethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-prolinate



101-7 101-8

This compound was prepared using a similar procedure as described as step1 in example 1, with compound 101-7 replacing compound a-6. The crude product was further purified by Silica gel column to get the title compound.

Step 9: Preparation of ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)-6-(trifluoromethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline

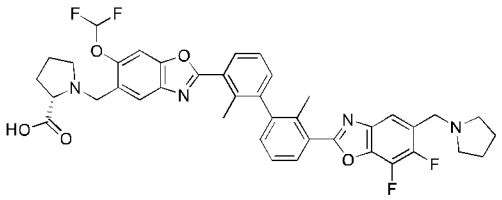


101-8 compound 101

This compound was prepared using similar procedures as described as step 5 in example 1, with compound 101-8 replacing compound 1-4. The mixture was concentrated under reduced pressure to get the title compound. LC-MS(m/z):761.3$(M+H)^+$.

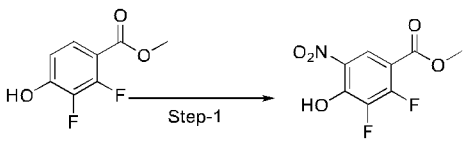
Example 102 Synthesis of Compound 102

((2-(3'-(6,7-difluoro-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline



Compound 102

Step 1: Preparation of methyl 2,3-difluoro-4-hydroxy-5-nitrobenzoate



102-1

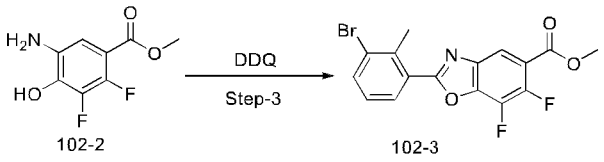
This compound was prepared using similar procedures as described as step1 in example A, with methyl 2,3-difluoro-4-hydroxybenzoate replacing compound a-1. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate) to get the title compound.

Step 2: Preparation of methyl 5-amino-2,3-difluoro-4-hydroxybenzoate

102-1 102-2

This compound was prepared using similar procedures as described as step2 in example A, with compound 102-1 replacing compound a-2. The filtrate was concentrate under reduced pressure and the title compound was obtained.

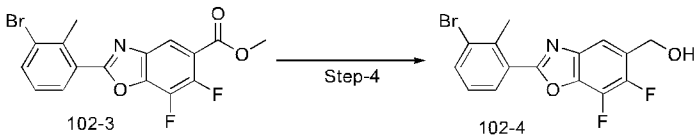
Step 3: Preparation of methyl 2-(3-bromo-2-methylphenyl)-6,7-difluorobenzo[d]oxazole-5-carboxylate



102-2 102-3

This compound was prepared using similar procedures as described as step3 in example A, with compound 102-2 replacing compound a-3. The crude product was dissolved in methanol, filtered and dried in a vacuum oven. The title compound was obtained.

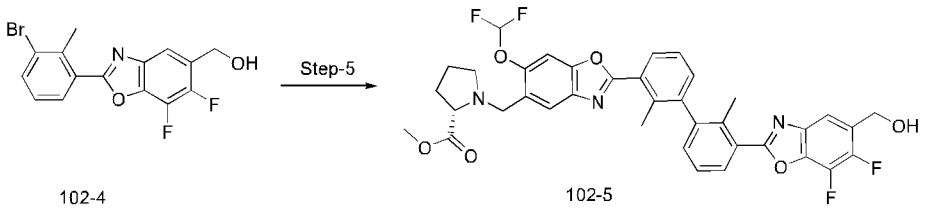
Step 4: Preparation of (2-(3-bromo-2-methylphenyl)-6,7-difluorobenzo[d]oxazol-5-yl)methanol



102-3 102-4

This compound was prepared using a similar procedure as described as step5 in example A, with compound 102-3 replacing compound a-5. The filtrate was concentrate under reduced pressure and the title compound was obtained.

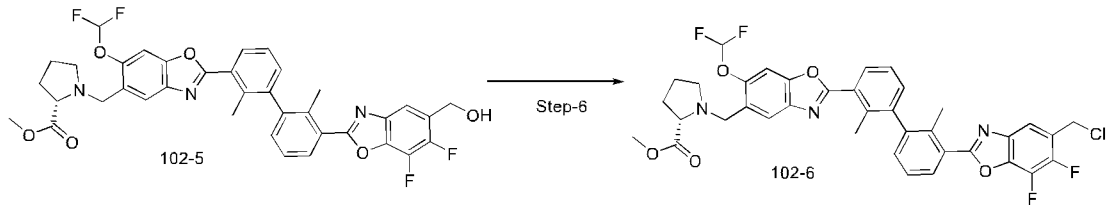
Step 5: Preparation of methyl ((2-(3'-(6,7-difluoro-5-(hydroxymethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-prolinate



102-4 102-5

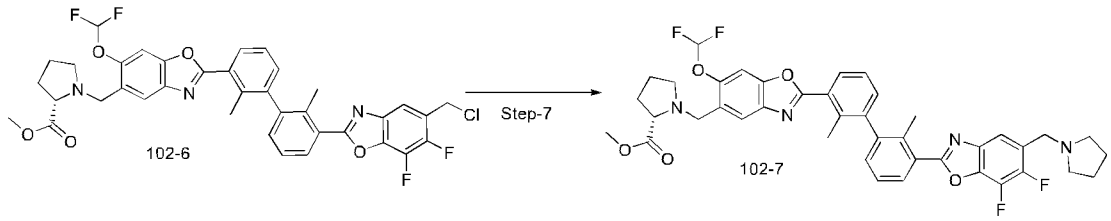
This compound was prepared using a similar procedure as described as step1 in example 1, with compound 102-4 replacing compound a-6. The crude product was further purified by Silica gel column to get title compound.

Step 6: Preparation of methyl ((2-(3'-(5-(chloromethyl)-6,7-difluorobenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-prolinate



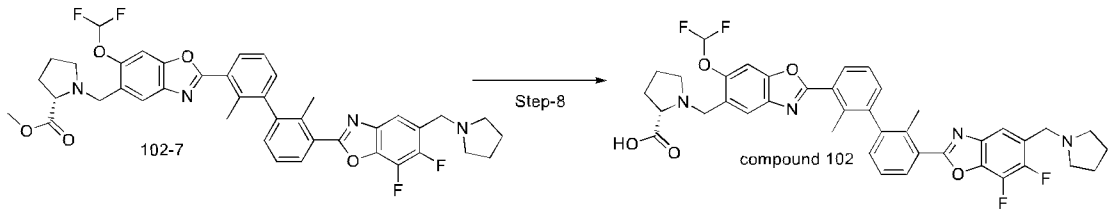
This compound was prepared using a similar procedure as described as step2 in example 1, with compound 102-5 replacing compound 1-1. The crude product was used directly in the next step.

Step 7: Preparation of methyl ((2-(3'-(6,7-difluoro-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-prolinate



This compound was prepared using a similar procedure as described as step3 in example 1, with compound 102-6 replacing compound 1-2, and with pyrrolidine replacing (1S, 2R)-2-aminocyclopentan-1-ol. The crude product was further purified by Silica gel column (PE/EA) to get title compound.

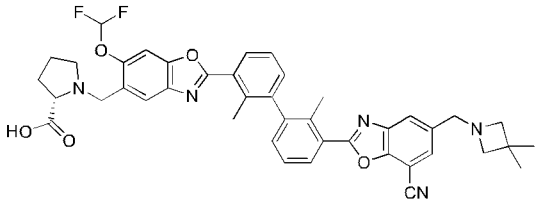
Step 8: Preparation of ((2-(3'-(6,7-difluoro-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline



This compound was prepared using a similar procedure as described as step5 in example 1 with compound 102-7 replacing compound 1-4. The crude product was further purified by Silica gel column to get title compound. LC-MS(m/z):729.3$(M+H)^+$. 1H NMR (500 MHz, DMSO-d6) δ8.21 (dd, J = 7.9, 1.4 Hz, 1H), 8.19 – 8.14 (m, 2H), 8.08 (s, 1H), 7.82 (s, 1H), 7.62-7.54 (m, 2H), 7.51-7.44 (m, 2H), 7.40 (t, J = 71.9 Hz, 1H), 4.58 (s, 2H), 4.36-4.20 (m, 2H), 3.91 (s, 1H), 3.46 (s, 3H), 3.20-3.07 (m, 2H), 2.96 (s, 1H), 2.45 (d, J = 4.0 Hz, 6H), 2.35-2.25 (m, 1H), 2.08-1.76(m, 8H).

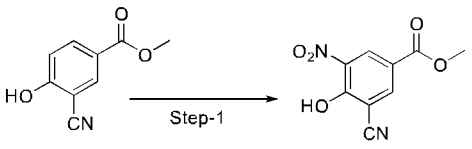
Example 103 Synthesis of Compound 103

((2-(3'-(7-cyano-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline



Compound 103

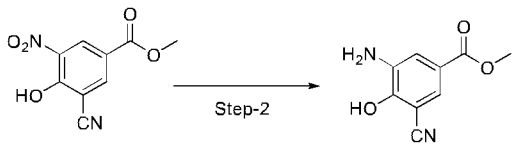
Step 1: Preparation of methyl 3-cyano-4-hydroxy-5-nitrobenzoate



103-1

This compound was prepared using similar procedures as described as step1 in example A, with Methyl 3-cyano-4-hydroxybenzoate replacing compound a-1. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate) and the title compound was obtained.

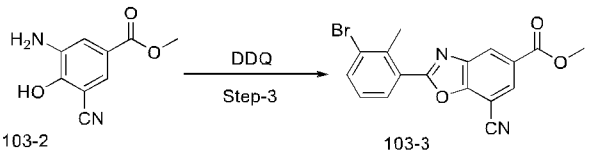
Step 2: Preparation of methyl 3-amino-5-cyano-4-hydroxybenzoate



103-1 103-2

This compound was prepared using similar procedures as described as step2 in example A, with compound 103-1 replacing compound a-2. The filtrate was concentrate under reduced pressure and the title compound was obtained.

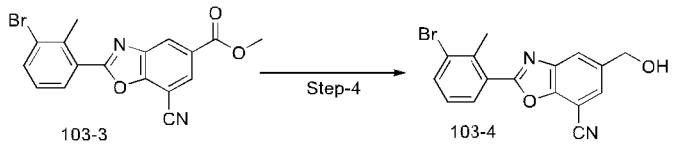
Step 3: Preparation of methyl 2-(3-bromo-2-methylphenyl)-7-cyanobenzo[d]oxazole-5-carboxylate



103-2 103-3

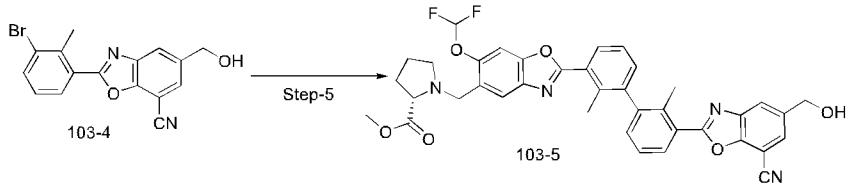
This compound was prepared using similar procedures as described as step3 in example A, with compound 103-2 replacing compound a-3. The crude product was further purified by Silica gel column to get the title compound.

Step 4: Preparation of 2-(3-bromo-2-methylphenyl)-5-(hydroxymethyl)benzo[d]oxazole-7-carbonitrile



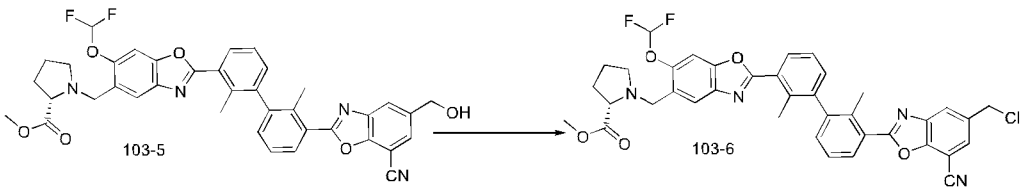
This compound was prepared using similar procedures as described as step5 in example A, with compound 103-3 replacing compound a-5. The filtrate was concentrate under reduced pressure to get the title compound.

Step 5: Preparation of methyl ((2-(3'-(7-cyano-5-(hydroxymethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-prolinate



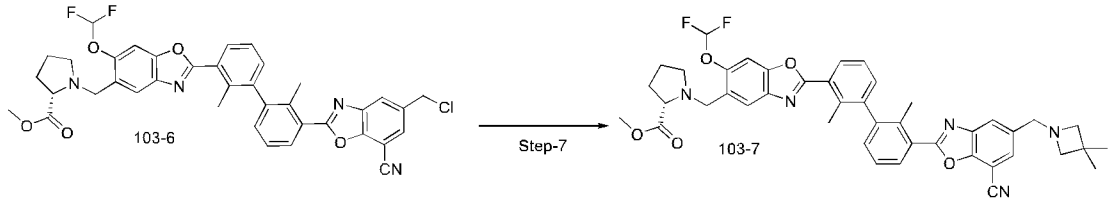
This compound was prepared using similar procedures as described as step1 in example 1 with compound 103-4 replacing compound a-6. The crude product was further purified by Silica gel column to get the title compound.

Step 6: Preparation of methyl ((2-(3'-(5-(chloromethyl)-7-cyanobenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-prolinate



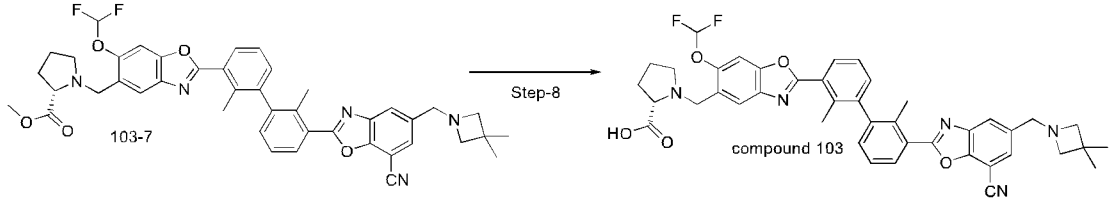
This compound was prepared using a similar procedure as described as step2 in example 1, with compound 103-5 replacing compound 1-1. The crude product was used directly in the next step.

Step 7: Preparation of methyl ((2-(3'-(7-cyano-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-prolinate



This compound was prepared using a similar procedure as described as step3 in example 1, with compound 103-6 replacing compound 1-2, and with 3,3-dimethylazetidine replacing (1S, 2R)-2-aminocyclopentan-1-ol. The crude product was further purified by Silica gel column (PE/EA) to get the title compound.

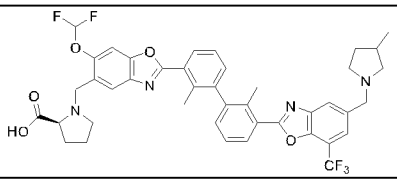
Step 8: Preparation of ((2-(3'-(7-cyano-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline

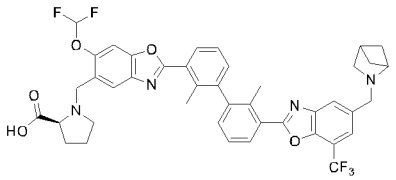
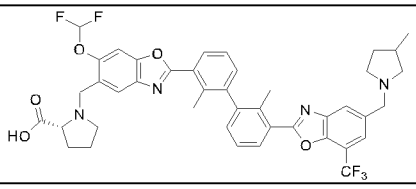
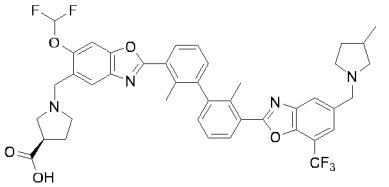
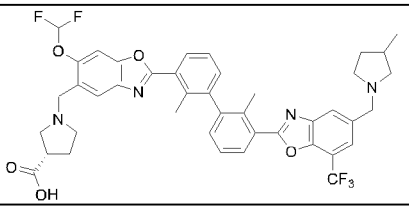
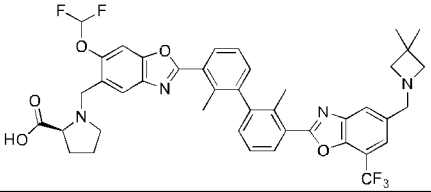
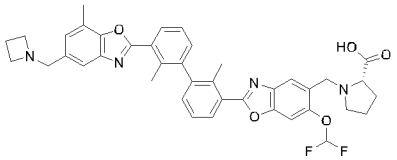
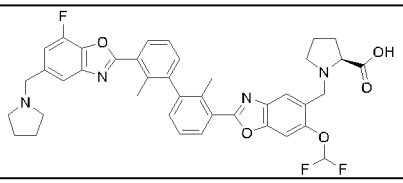
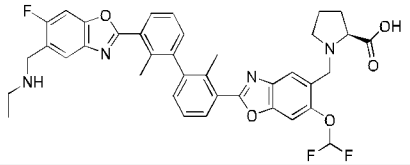
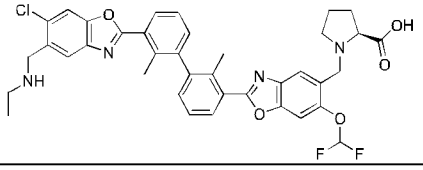
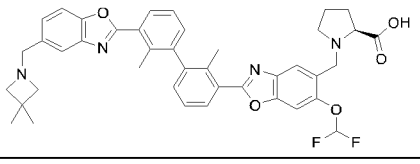


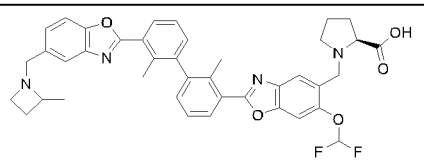
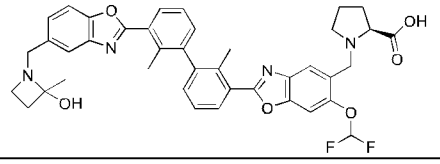
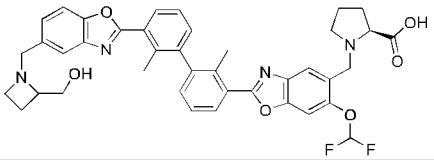
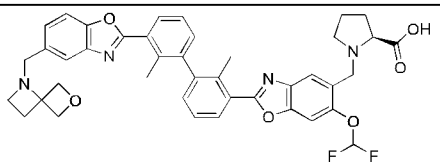
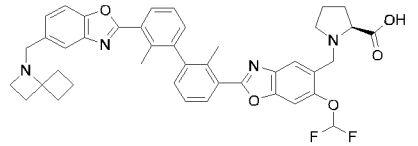
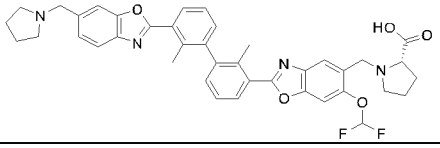
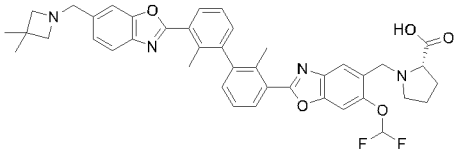
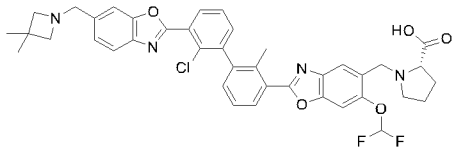
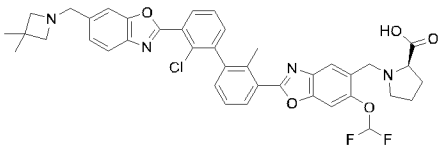
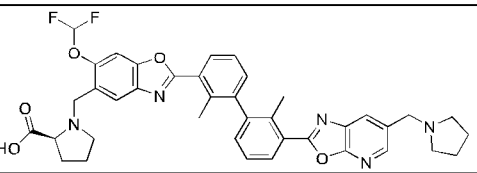
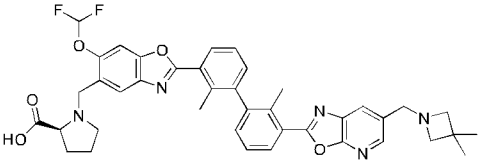
This compound was prepared using similar procedures as described as step 5 in example 1 with compound 103-7 replacing compound 1-4. The crude product was further purified by Silica gel column to get the title compound. LC-MS(m/z):732.3$(M+H)^+$. 1H NMR (500 MHz, DMSO-*d6*) 8.20 (dd, *J* = 7.9, 1.4 Hz, 1H), 8.16 (dd, *J* = 7.9, 1.5 Hz, 1H), 8.09 (s, 1H), 7.97 (s, 1H), 7.85 (s, 1H), 7.73 (s, 1H), 7.62 – 7.51 (m, 2H), 7.50 – 7.41 (m, 2H), 7.38 (t, *J* = 71.9 Hz, 1H), 3.96 (s,2H),3.75 (s, 2H), 3.36 (dd, *J* = 9.1, 5.4 Hz, 1H), 3.07 (td, *J* = 9.4, 8.4, 3.3 Hz, 1H), 2.99 (s,3H), 2.56 (q, *J* = 8.5 Hz, 1H), 2.44 (d, 6H, *J* = 2.5Hz), 2.17-2.08 (m, 1H), 1.90 – 1.68 (m, 4H), 1.20 (s, 6H).

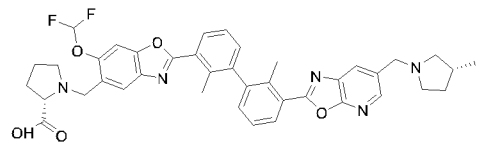
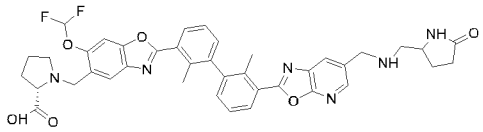
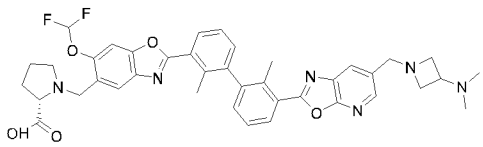
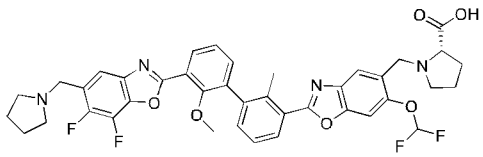
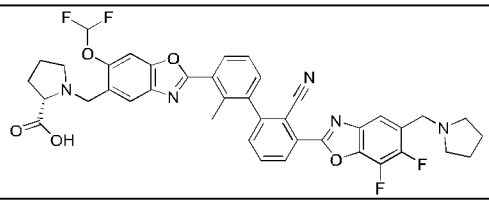
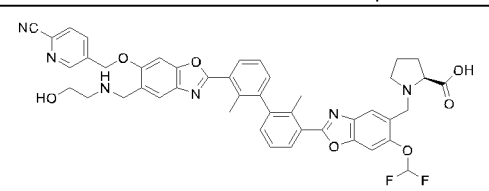
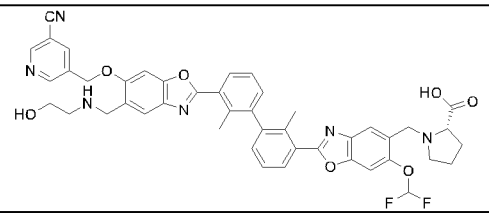
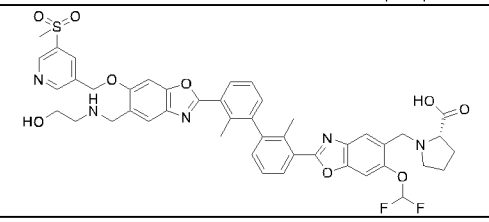
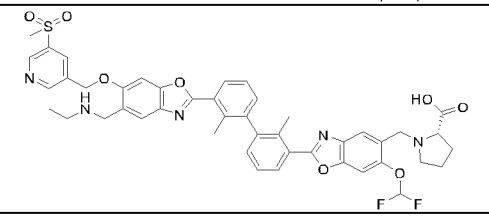
The compounds of table 2 were prepared in a similar manner to Examples 100-103 via different reaction starting materials and suitable reagents.

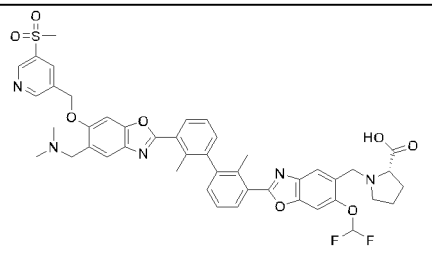
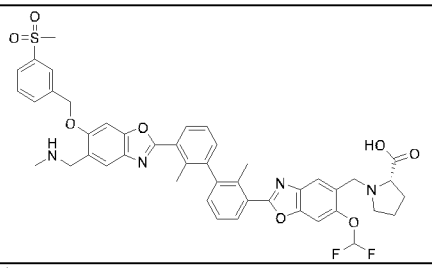
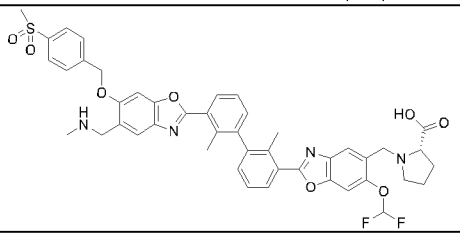
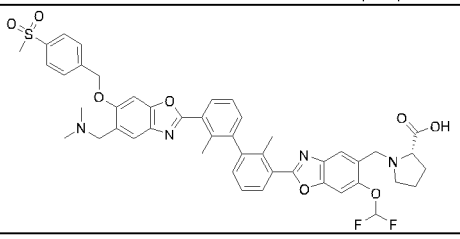
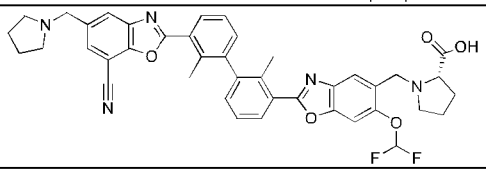
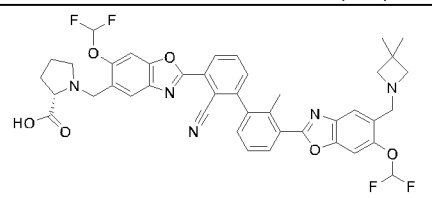
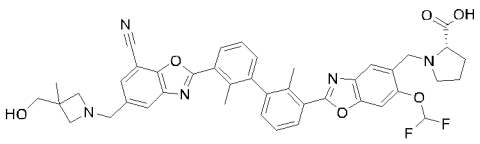
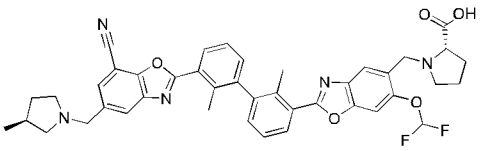
Table 2

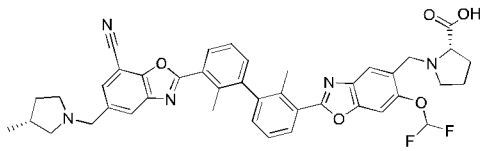
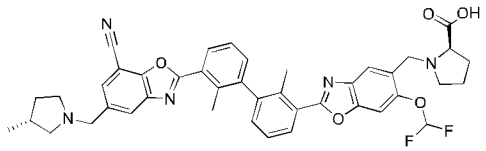
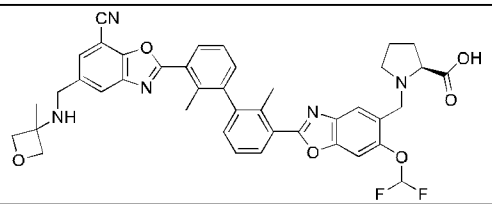
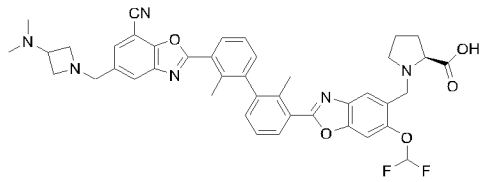
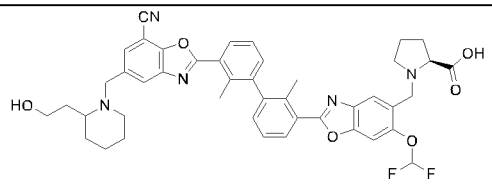
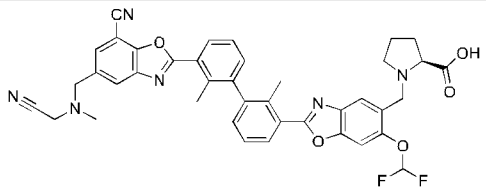
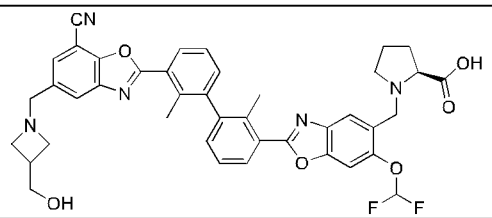
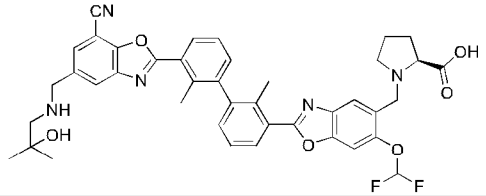
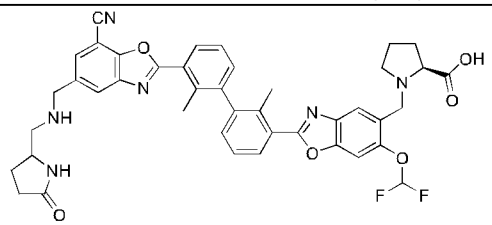
EX No.	Chemical Name	Structure	Physical Data (MS) $(M+H)^+$
88	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((3-methylpyrrolidin-1-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		775.3

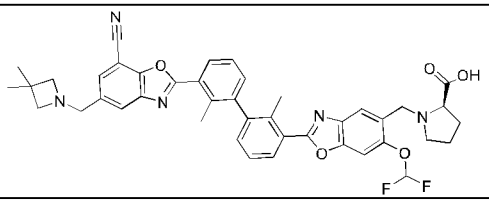
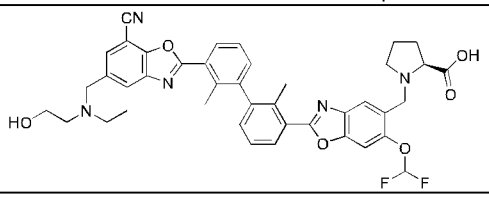
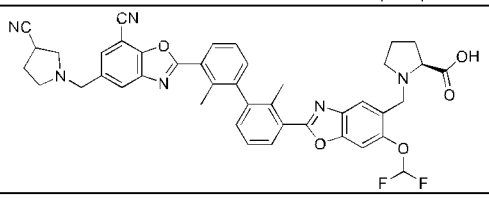
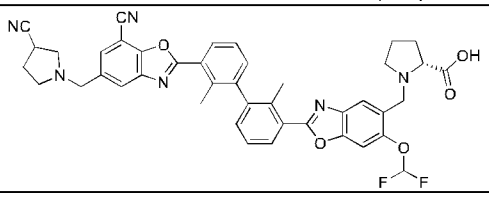
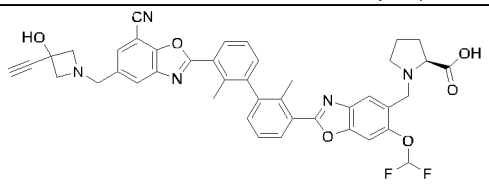
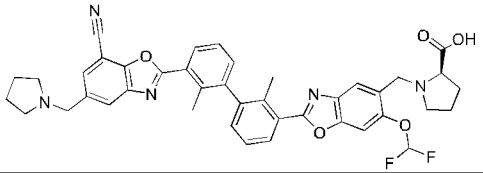
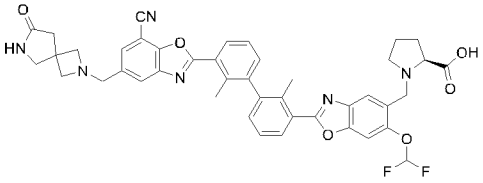
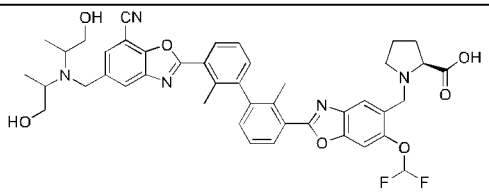
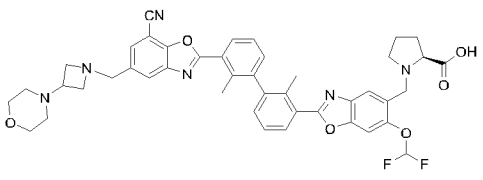
89	((2-(3'-(5-((2-azabicyclo[2.1.1]hexan-2-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		773.3
90	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((3-methylpyrrolidin-1-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-D-proline		775.3
91	(3R)-1-((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((3-methylpyrrolidin-1-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid		775.3
92	(3S)-1-((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((3-methylpyrrolidin-1-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid		775.3
93	((6-(difluoromethoxy)-2-(3'-(5-((3,3-dimethylazetidin-1-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		775.3
94	((2-(3'-(5-(azetidin-1-ylmethyl)-7-methylbenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		693.3
95	((6-(difluoromethoxy)-2-(3'-(7-fluoro-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		711.3
96	((6-(difluoromethoxy)-2-(3'-(5-((ethylamino)methyl)-6-fluorobenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		685.3
97	((2-(3'-(6-chloro-5-((ethylamino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		701.2
312	((6-(difluoromethoxy)-2-(3'-(5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		707.3

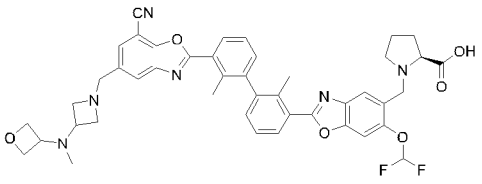
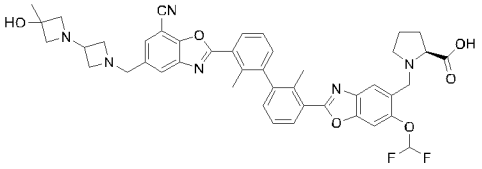
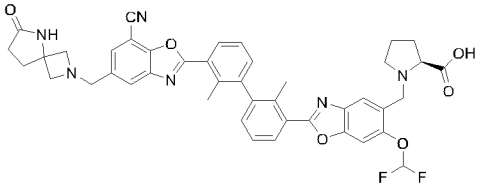
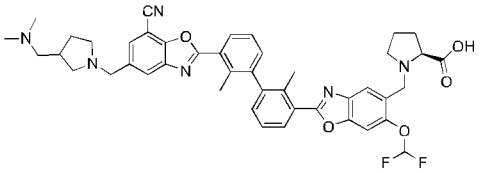
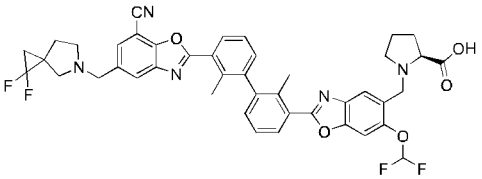
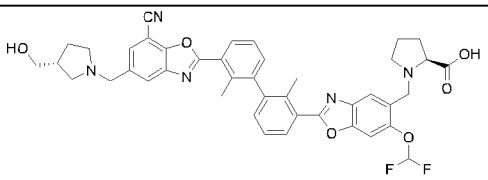
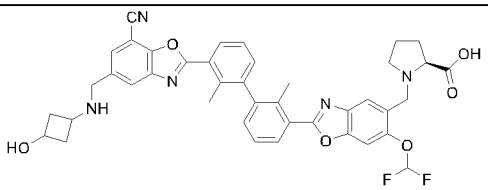
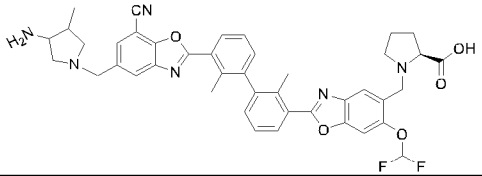
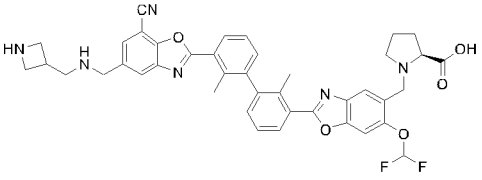
313	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((2-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		693.3
104	((6-(difluoromethoxy)-2-(3'-(5-((2-hydroxy-2-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		709.3
105	((6-(difluoromethoxy)-2-(3'-(5-((2-(hydroxymethyl)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		709.3
106	((2-(3'-(5-((6-oxa-1-azaspiro[3.3]heptan-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		721.3
107	((2-(3'-(5-((1-azaspiro[3.3]heptan-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		719.3
108	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(6-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		693.3
109	((6-(difluoromethoxy)-2-(3'-(6-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		707.3
110	((2-(2'-chloro-3'-(6-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		727.3
111	((2-(2'-chloro-3'-(6-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline		727.3
112	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(6-(pyrrolidin-1-ylmethyl)oxazolo[5,4-b]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		694.3
113	((6-(difluoromethoxy)-2-(3'-(6-((3,3-dimethylazetidin-1-yl)methyl)oxazolo[5,4-b]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		708.3

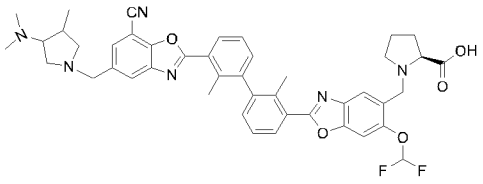
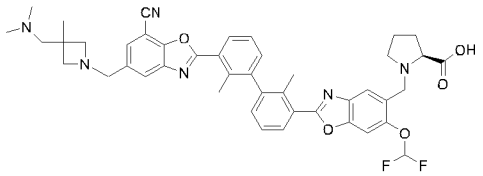
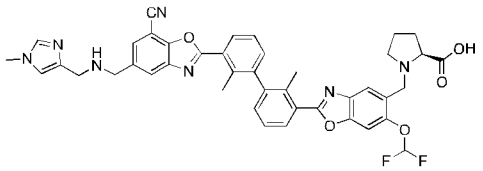
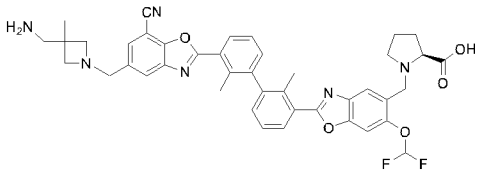
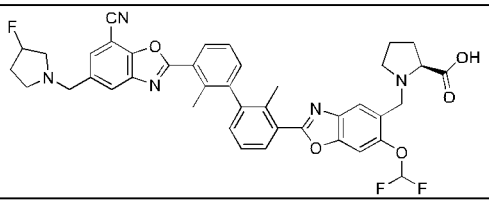
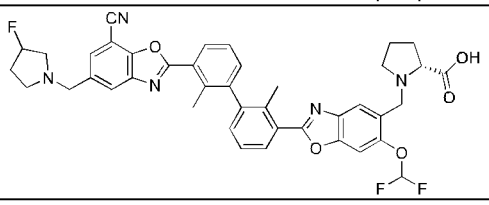
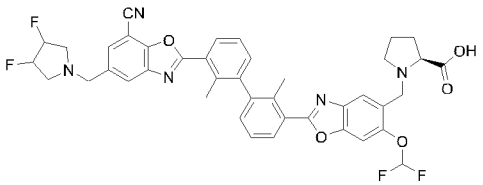
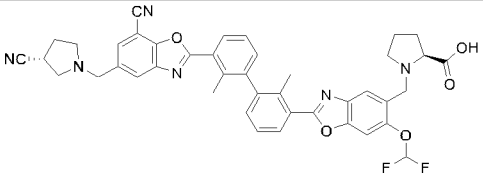
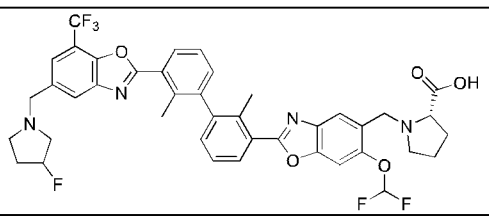
114	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(6-(((R)-3-methylpyrrolidin-1-yl)methyl)oxazolo[5,4-b]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		708.3
115	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(6-((((5-oxopyrrolidin-2-yl)methyl)amino)methyl)oxazolo[5,4-b]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		737.3
116	((6-(difluoromethoxy)-2-(3'-(6-((3-(dimethylamino)azetidin-1-yl)methyl)oxazolo[5,4-b]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		723.3
117	((2-(3'-(6,7-difluoro-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2'-methoxy-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		745.3
118	((2-(2'-cyano-3'-(6,7-difluoro-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		740.2
119	((2-(3'-(6-((6-cyanopyridin-3-yl)methoxy)-5-(((2-hydroxyethyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		815.3
120	((2-(3'-(6-((5-cyanopyridin-3-yl)methoxy)-5-(((2-hydroxyethyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		815.3
121	((6-(difluoromethoxy)-2-(3'-(5-(((2-hydroxyethyl)amino)methyl)-6-((5-(methylsulfonyl)pyridin-3-yl)methoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		868.3
122	((6-(difluoromethoxy)-2-(3'-(5-((ethylamino)methyl)-6-((5-(methylsulfonyl)pyridin-3-yl)methoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		852.3

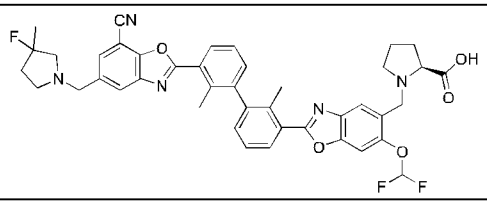
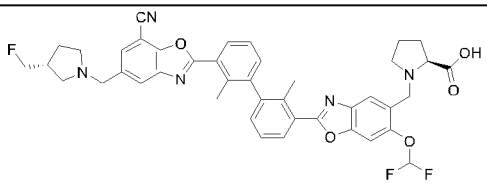
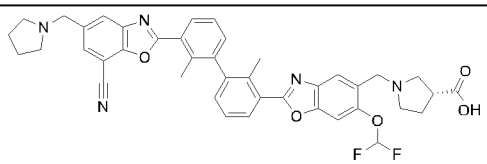
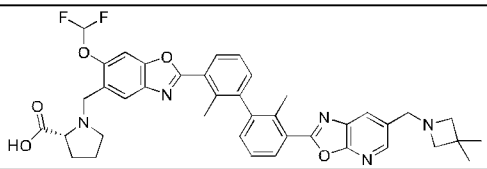
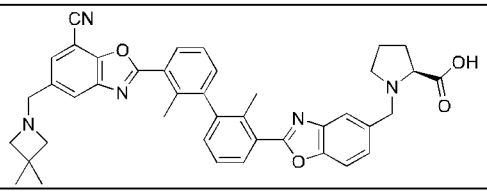
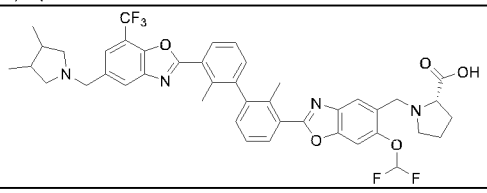
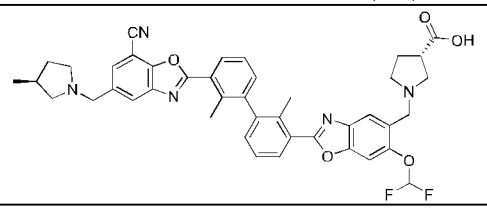
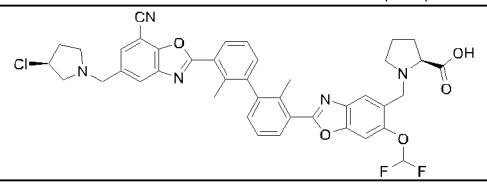
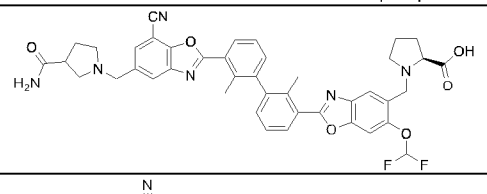
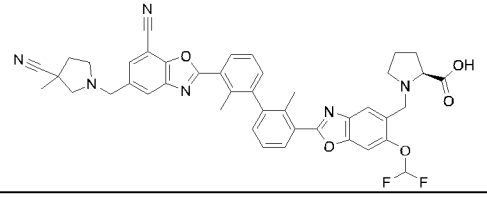
123	((6-(difluoromethoxy)-2-(3'-(5-((dimethylamino)methyl)-6-((5-(methylsulfonyl)pyridin-3-yl)methoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		852.3
124	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((methylamino)methyl)-6-((3-(methylsulfonyl)benzyl)oxy)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		837.3
125	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((methylamino)methyl)-6-((4-(methylsulfonyl)benzyl)oxy)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		837.3
126	((6-(difluoromethoxy)-2-(3'-(5-((dimethylamino)methyl)-6-((4-(methylsulfonyl)benzyl)oxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		851.3
127	((2-(3'-(7-cyano-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		718.3
128	((2-(2-cyano-3'-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2'-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		784.3
129	((2-(3'-(7-cyano-5-((3-(hydroxymethyl)-3-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		748.3
130	((2-(3'-(7-cyano-5-(((S)-3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		732.3

131	((2-(3'-(7-cyano-5-(((R)-3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		732.3
132	((2-(3'-(7-cyano-5-(((R)-3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline		732.3
133	((2-(3'-(7-cyano-5-(((3-methyloxetan-3-yl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		734.3
134	((2-(3'-(7-cyano-5-((3-(dimethylamino)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		747.3
135	((2-(3'-(7-cyano-5-((2-(2-hydroxyethyl)piperidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		776.3
136	((2-(3'-(7-cyano-5-(((cyanomethyl)(methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		717.3
137	((2-(3'-(7-cyano-5-((3-(hydroxymethyl)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		734.3
138	((2-(3'-(7-cyano-5-(((2-hydroxy-2-methylpropyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		736.3
139	((2-(3'-(7-cyano-5-((((5-oxopyrrolidin-2-yl)methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		761.3

140	((2-(3'-(7-cyano-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline		732.3
141	((2-(3'-(7-cyano-5-((ethyl(2-hydroxyethyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		736.3
142	((2-(3'-(7-cyano-5-((3-cyanopyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		743.3
143	((2-(3'-(7-cyano-5-((3-cyanopyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline		743.3
144	((2-(3'-(7-cyano-5-((3-ethynyl-3-hydroxyazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		744.3
145	((2-(3'-(7-cyano-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline		718.3
146	((2-(3'-(7-cyano-5-((7-oxo-2,6-diazaspiro[3.4]octan-2-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		773.3
147	((2-(3'-(5-((bis(1-hydroxypropan-2-yl)amino)methyl)-7-cyanobenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		780.3
148	((2-(3'-(7-cyano-5-((3-morpholinoazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		789.3

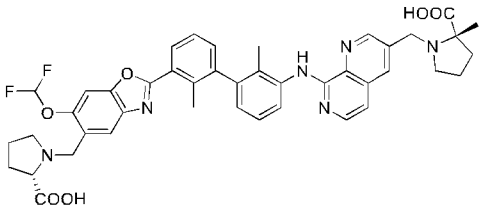
149	((2-(3'-(7-cyano-5-((3-(methyl(oxetan-3-yl)amino)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		789.3
150	((2-(3'-(7-cyano-5-((3-hydroxy-3-methyl-[1,3'-biazetidin]-1'-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		789.3
151	((2-(3'-(7-cyano-5-((6-oxo-2,5-diazaspiro[3.4]octan-2-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		773.3
152	((2-(3'-(7-cyano-5-((3-((dimethylamino)methyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		775.3
153	((2-(3'-(7-cyano-5-((1,1-difluoro-5-azaspiro[2.4]heptan-5-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		780.3
154	((2-(3'-(7-cyano-5-(((R)-3-(hydroxymethyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		748.3
155	((2-(3'-(7-cyano-5-(((3-hydroxycyclobutyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		734.3
156	((2-(3'-(5-((3-amino-4-methylpyrrolidin-1-yl)methyl)-7-cyanobenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		747.3
157	((2-(3'-(5-(((azetidin-3-ylmethyl)amino)methyl)-7-cyanobenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		733.3

158	((2-(3'-(7-cyano-5-((3-(dimethylamino)-4-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		775.3
159	((2-(3'-(7-cyano-5-((3-((dimethylamino)methyl)-3-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		775.3
160	((2-(3'-(7-cyano-5-((((1-methyl-1H-imidazol-4-yl)methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		758.3
161	((2-(3'-(5-((3-(aminomethyl)-3-methylazetidin-1-yl)methyl)-7-cyanobenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		747.3
162	((2-(3'-(7-cyano-5-((3-fluoropyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		736.3
163	((2-(3'-(7-cyano-5-((3-fluoropyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline		736.3
164	((2-(3'-(7-cyano-5-((3,4-difluoropyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		754.3
165	((2-(3'-(7-cyano-5-(((R)-3-cyanopyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		743.3
166	((6-(difluoromethoxy)-2-(3'-(5-((3-fluoropyrrolidin-1-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		779.3

167	((2-(3'-(7-cyano-5-((3-fluoro-3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		750.3
168	((2-(3'-(7-cyano-5-(((R)-3-(fluoromethyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		750.3
169	(R)-1-((2-(3'-(7-cyano-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid		718.3
170	((6-(difluoromethoxy)-2-(3'-(6-((3,3-dimethylazetidin-1-yl)methyl)oxazolo[5,4-b]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-D-proline		708.3
318	((2-(3'-(7-cyano-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		666.3
84	((6-(difluoromethoxy)-2-(3'-(5-((3,4-dimethylpyrrolidin-1-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		789.3
259	(S)-1-((2-(3'-(7-cyano-5-(((S)-3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid		732.3
261	((2-(3'-(5-(((S)-3-chloropyrrolidin-1-yl)methyl)-7-cyanobenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		752.2
315	((2-(3'-(5-((3-carbamoylpyrrolidin-1-yl)methyl)-7-cyanobenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		761.3
316	((2-(3'-(7-cyano-5-((3-cyano-3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		757.3

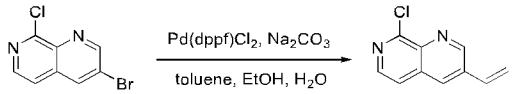
Example 171 Synthesis of compound 171

(S)-1-((8-((3'-(5-(((S)-2-carboxypyrrolidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)amino)-1,7-naphthyridin-3-yl)methyl)-2-methylpyrrolidine-2-carboxylic acid



Compound 171

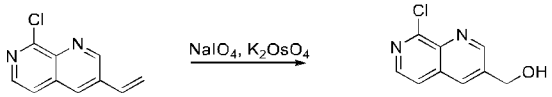
Step 1: Preparation of 8-chloro-3-vinyl-1,7-naphthyridine



171-1 171-2

To a solution of compound 171-1 (2.43 g) in toluene (30 mL), EtOH (10 mL), 10% Na_2CO_3 aq. (10 mL) and $Pd(dppf)Cl_2$.DCM (420 mg) was added. And then 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (3.1 g) was added dropwise under N_2 protection. The mixture was allowed to stir at 100 °C for 16 h. The reaction was quenched with H_2O (50 mL) and extracted by EtOAc for 3 times. The organic layers were combined and washed with brine. The resulting solution was concentrated and purified by silicagel (eluting with hexane-EtOAc using a gradient from 8:1 to 5:1) to afford 8-chloro-3-vinyl-1,7-naphthyridine (1.1 g) as a brown solid.

Step 2: Preparation of (8-chloro-1,7-naphthyridin-3-yl)methanol



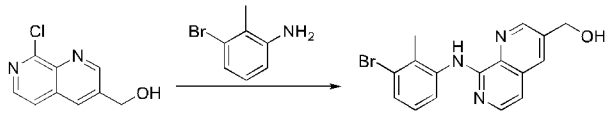
171-2 171-3

To a solution of compound 171-2 (380 mg) in 1,4-dioxane (20 mL)/water (20 mL), K_2OsO_4 (4.0 mg) was added and stirred for 30 min at room temperature. $NaIO_4$ (1.0 g) was added in small portions at the same temperature. After stirring for 3 h, the reaction mixture was quenched with saturated $Na_2S_2O_3$ solution and extracted with DCM (40 mL) for 3 times. The organic layers were combined and dried over Na_2SO_4. The resulting solution was concentrated to afford 8-chloro-1,7-naphthyridine-3-carbaldehyde.

The above 8-chloro-1,7-naphthyridine-3-carbaldehyde (320 mg) was dissolved in 20 mL MeOH, and $NaBH_4$ (200 mg) was added in one portion. The resulting mixture was stirred for 2h at room temperature then quenched with water (30 mL). The mixture was extracted with DCM (20 mL) for 3 times and the organic phases were dried over Na_2SO_4. The resulting solution was

concentrated and purified by silicagel (eluting with DCM-EtOAc using a gradient from 1:1 to 1:2) to afford (8-chloro-1,7-naphthyridin-3-yl)methanol (240 mg) as a white solid.

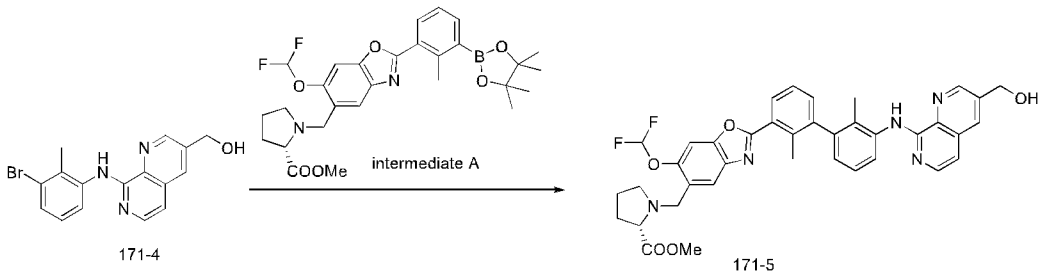
Step 3: Preparation of (8-((3-bromo-2-methylphenyl)amino)-1,7-naphthyridin-3-yl)methanol



171-3 171-4

To a microwave reaction vial were added 3-bromo-2-methylaniline (2.50 g), compound 171-3 (1.86 g), *t*-BuOH (15 mL) and HCl (4.0 M in 1,4-dioxane, 3 mL). The vial was capped and the reaction mixture was heated at 100 °C for 4 h in microwave oven. It was diluted with 20 mL of water and then extracted with DCM (50 ml×2). The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated in vacue. The residue was concentrated and recrystallized by DCM: Hexane (1:1) to afford (8-((3-bromo-2-methylphenyl)amino)-1,7-naphthyridin-3-yl)methanol (2.0 g) as an off-white solid.

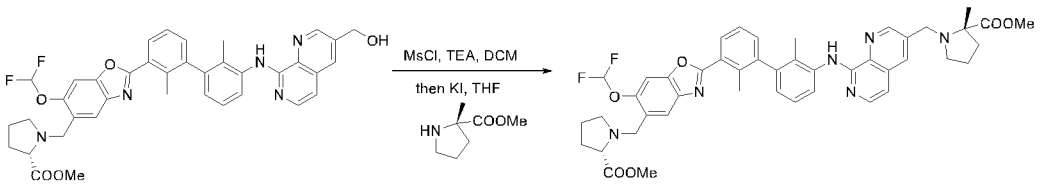
Step 4: Preparation of methyl ((5-(difluoromethoxy)-2-(3'-((3-(hydroxymethyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-6-yl)methyl)-L-prolinate



171-4 171-5

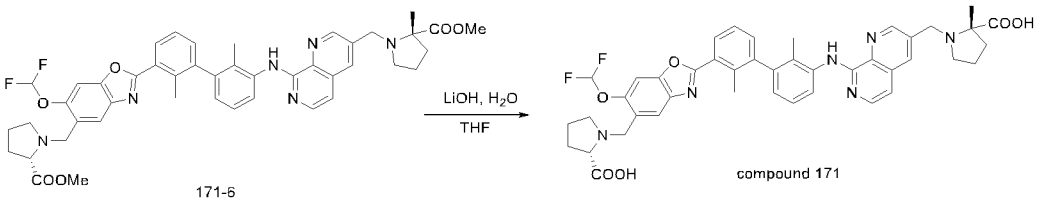
To a solution of compound 171-4 (0.69 g), intermediate A (1.5 g) in toluene (15 mL), EtOH (5 mL), 10% Na_2CO_3 aq. (5 mL), $Pd(dppf)Cl_2$.DCM (78 mg) was added under N_2 protection. The mixture was allowed to stir at 110 °C overnight. The reaction was quenched with H_2O (20 mL) and extracted by EtOAc (50 mL) for 3 times. The organic layers were combined and washed with brine. The resulting solution was concentrated and purified by silicagel (eluting with Hexane-EtOAc using a gradient from 3:1 to 1:1) to afford compound 171-5 (0.88 g) as a brown oil.

Step 5: Preparation of methyl (S)-1-((8-((3'-(6-(difluoromethoxy)-5-(((S)-2-(methoxycarbonyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)amino)-1,7-naphthyridin-3-yl)methyl)-2-methylpyrrolidine-2-carboxylate.



To a solution of compound 171-5 (250 mg) and TEA (100 mg) in DCM (5.0 mL), MsCl (89 mg) was added dropwise at 0 °C. The reaction was allowed to stir at room temperature for 4 hrs. The resulting mixture was concentrated under vacuo and redissolved by THF (5 mL). Methyl (S)-2-methylpyrrolidine-2-carboxylate (143 mg) and KI (1 mg) was added to the solution and then the reaction was continued to stir at room temperature overnight unstill above methanesulfonate was consumed. The residue was concentrated and purified directly by RP-column (mobile phase: MeCN : water = 10:90 with 0.1% HCl) to afford compound 171-6 (105 mg) as an off-white solid.

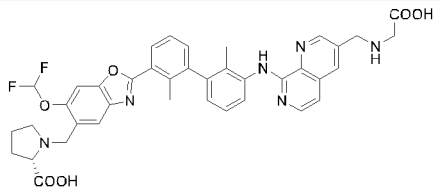
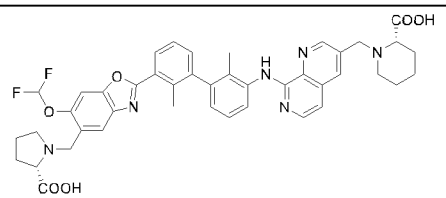
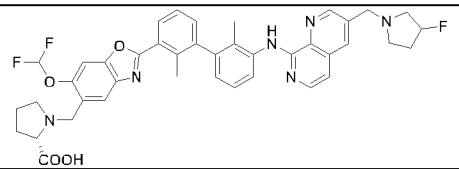
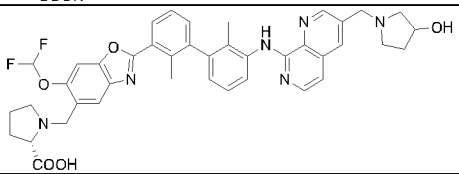
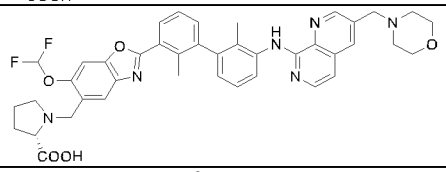
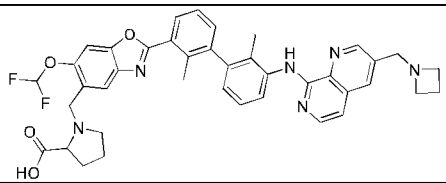
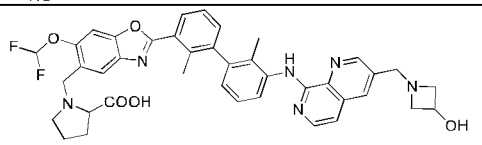
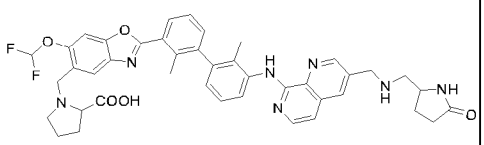
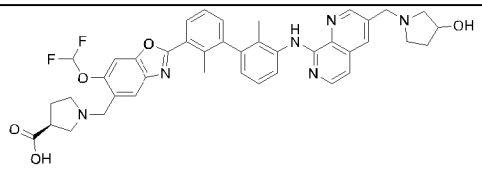
Step 6: Preparation of (S)-1-((8-((3'-(5-(((S)-2-carboxypyrrolidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)amino)-1,7-naphthyridin-3-yl)methyl)-2-methylpyrrolidine-2-carboxylic acid

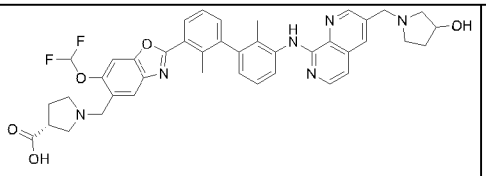
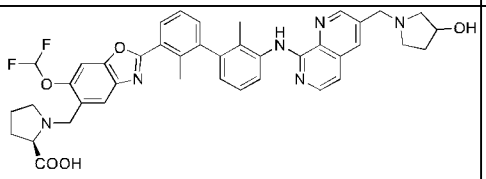
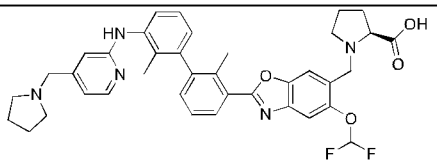


To a solution of compound 171-6 (105 mg) in THF/water = 1:1 (4 mL) was added LiOH (40 mg). The resulting mixture was stirred for 24 h at room temperature. THF layer was separated and purified by RP-column (mobile phase: MeCN : water (0.1% HCl) using a gradient from 10:90 to 30:70) to afford 78 mg (S)-1-((8-((3'-(5-(((S)-2-carboxypyrrolidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)amino)-1,7-naphthyridin-3-yl)methyl)-2-methylpyrrolidine-2-carboxylic acid (compound 171). LC-MS(m/z):777.3$(M+H)^+$. 1H NMR (500 MHz, Methanol-d4) δ 9.23 (d, 1H, J = 2.1 Hz), 8.60 (d, 1H, J = 2.0 Hz), 8.20 (dd, 1H, J = 7.9, 1.5 Hz), 8.07 (s, 1H), 7.76 (s, 1H), 7.69–7.63 (m, 2H), 7.57 (t, 1H, J = 7.8 Hz), 7.53 (t, 1H, J = 7.7 Hz), 7.46 (dd, 1H, J = 7.6, 1.5 Hz), 7.38 (dd, 1H, J = 7.6, 1.4 Hz), 7.35 (d,1H, J = 6.9 Hz), 7.12 (t, 1H, J_{F-H} = 72.6 Hz), 4.83 (d, 1H, J = 13.2 Hz), 4.74 (d, 1H, J = 13.3 Hz), 4.62 (d, 1H, J = 13.2 Hz), 4.49 (d, 1H, J = 13.2 Hz), 4.33 (dd, 1H, J = 9.6, 7.2 Hz), 3.66-3.62 (m, 1H), 3.52–3.37 (m, 3H), 2.63–2.56 (m, 1H), 2.55 (s, 3H), 2.41–2.32 (m, 1H), 2.29–2.14 (m, 4H), 2.09 (s, 3H), 2.06–1.98 (m, 2H), 1.75 (s, 3H).

The compounds of table 3 were prepared in a similar manner to Example 171 via different reaction starting materials and suitable reagents.

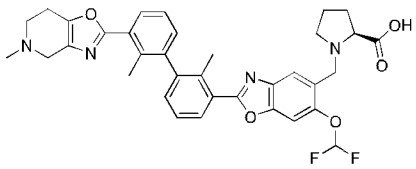
Table 3

EX No.	Chemical Name	Structure	Physical Data (MS) $(M+H)^+$
172	((2-(3'-((3-(((carboxymethyl)amino)methyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		723.3
173	(S)-1-((8-((3'-(5-(((S)-2-carboxypyrrolidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)amino)-1,7-naphthyridin-3-yl)methyl)piperidine-2-carboxylic acid		777.3
174	((6-(difluoromethoxy)-2-(3'-((3-((3-fluoropyrrolidin-1-yl)methyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		737.3
175	((6-(difluoromethoxy)-2-(3'-((3-((3-hydroxypyrrolidin-1-yl)methyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		735.3
176	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-((3-(morpholinomethyl)-1,7-naphthyridin-8-yl)amino)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		735.3
177	((2-(3'-((3-(azetidin-1-ylmethyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline		705.3
178	((6-(difluoromethoxy)-2-(3'-((3-((3-hydroxyazetidin-1-yl)methyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline		721.3
179	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-((3-((((5-oxopyrrolidin-2-yl)methyl)amino)methyl)-1,7-naphthyridin-8-yl)amino)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline		762.3
180	(3S)-1-((6-(difluoromethoxy)-2-(3'-((3-((3-hydroxypyrrolidin-1-yl)methyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid		735.3

181	(3R)-1-((6-(difluoromethoxy)-2-(3'-((3-((3-hydroxypyrrolidin-1-yl)methyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid		735.3
182	((6-(difluoromethoxy)-2-(3'-((3-((3-hydroxypyrrolidin-1-yl)methyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-D-proline		735.3
183	((5-(difluoromethoxy)-2-(2,2'-dimethyl-3'-((4-(pyrrolidin-1-ylmethyl)pyridin-2-yl)amino)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-6-yl)methyl)-L-proline		668.3

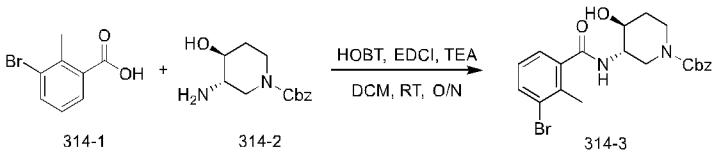
Example 314 Synthesis of Compound 314

((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-methyl-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline



Compound 314

Step 1: Preparation of benzyl (3S,4S)-3-(3-bromo-2-methylbenzamido)-4-hydroxypiperidine-1-carboxylate



314-1 314-2 314-3

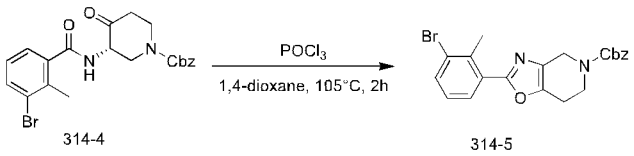
3-bromo-2-methylbenzoic acid (800 mg), benzyl (3S,4S)-3-amino-4-hydroxypiperidine-1-carboxylate (931.13 mg), EDCI (1.43 g), HOBT (1.01 g) and TEA (1.13 g) were added sequentially in DCM (50 mL), the mixture was stirred at room temperature overnight. The reaction solution was diluted with methylene chloride and washed sequentially with saturated aqueous sodium hydrogen carbonate and aqueous sodium chloride. The organic phase was dried with Na_2SO_4 and concentrated to white-like solid benzyl (3S,4S)-3-(3-bromo-2-methylbenzamido)-4-hydroxypiperidine-1-carboxylate (1.4 g, crude).

Step 2: Preparation of benzyl (S)-3-(3-bromo-2-methylbenzamido)-4-oxopiperidine-1-carboxylate

314-3 314-4

At room temperature, Dess-Martin (2.65 g) was batched into compound 314-3 (1.4 g) in DCM (30 mL) solution and stirred for 3 hrs. LC-MS determined that the reaction was completed; the reaction mixture was quenched with $Na_2S_2O_3$ solution and extracted with EA three times. The organic layers were washed with $NaHCO_3$ solution, dried over Na_2SO_4 and concentrated to get the benzyl (S)-3-(3-bromo-2-methylbenzamido)-4-oxopiperidine-1-carboxylate (1.1 g, crude) as light yellow solid.

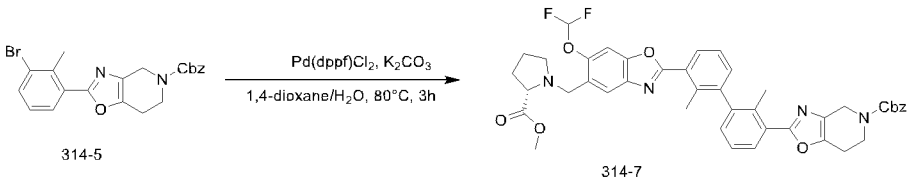
Step 3: Preparation of benzyl 2-(3-bromo-2-methylphenyl)-6,7-dihydrooxazolo[4,5-c]pyridine-5(4H)-carboxylate



314-4 314-5

A solution of $POCl_3$ (757.52 mg) in 1,4-dioxane (5 mL) was added dropwise to a solution of compound 314-4(891 mg) in 1,4-dioxane (15 mL). The temperature was then raised to 105 °C and stirring was continued for 2 hrs. The reaction mixture was slowly added dropwise to ice water and extracted with ethyl acetate. The organic phase was washed with saturated aqueous $NaHCO_3$ and saturated NaCl, dried over Na_2SO_4, and concentrated to get a residue, the residue was purified by chromatographic chromatography (DCM: MeOH = 20:1) to obtain white-like solid compound314-5 (800 mg).

Step 4: Preparation of benzyl (S)-2-(3'-(6-(difluoromethoxy)-5-((2-(methoxycarbonyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6,7-dihydrooxazolo[4,5-c]pyridine-5(4H)-carboxylate

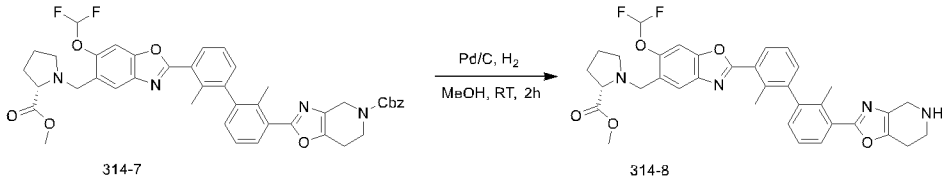


314-5 314-7

Compound 314-5 (800 mg), intermediate A (1015 mg), $Pd(dppf)Cl_2$ (343 mg) and K_2CO_3 (129.38 mg) were added to a mixture of 1,4-dixane (20 mL) and H_2O (5 mL). The reaction mixture was evacuated and fefilled three times using N_2, heated to 80 °C and stirred for 3 hrs. LC-MS monitored the reaction completely. The reaction mixture was concentrated and purified by TLC (PE: EA = 1:3) to obtain benzyl (S)-2-(3'-(6-(difluoromethoxy)-5-((2-

(methoxycarbonyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6,7-dihydrooxazolo[4,5-c]pyridine-5(4H)-carboxylate (800mg) as white-like solid.

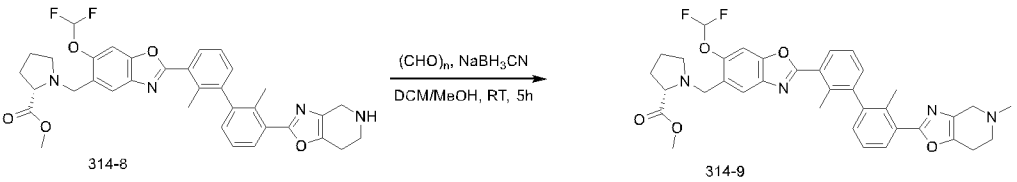
Step 5: Preparation of methyl ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-prolinate



314-7 314-8

Pd/C (200 mg) was added to a solution of compound 314-7 (800 mg) in MeOH (50 mL). The mixture was stirred at room temperature for 5 hrs under H_2 atmosphere. The reaction mixture was filtered and concentrated to obtain methyl ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-prolinate (500 mg, crude) as white-like solid.

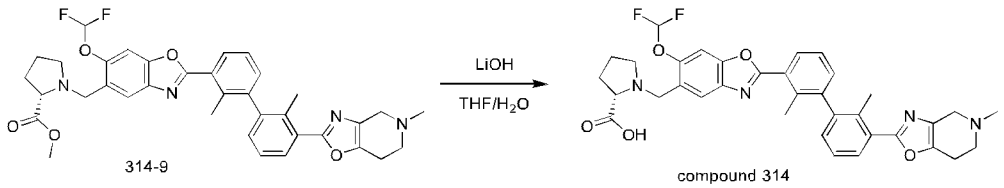
Step 6: Preparation of methyl ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-methyl-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-prolinate



314-8 314-9

$(CHO)_n$ (72 mg) was added to a solution of compound 314-8 (500 mg) in DCM (30 mL) and MeOH (10 mL). After the mixture was stirred for 30 min, $NaBH_3CN$ (150 mg) was added to the reaction solution in batches and stirred at room temperature overnight. The reaction was concentrated and purified by TLC (DCM:MeOH = 20:1) to obtain methyl ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-methyl-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-prolinate (400 mg) as white-like solid.

Step 7: Preparation of ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-methyl-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline

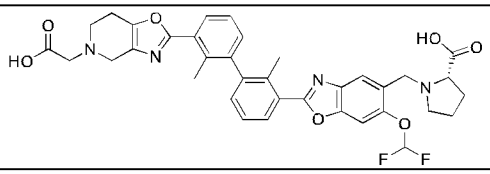
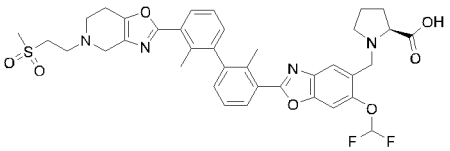
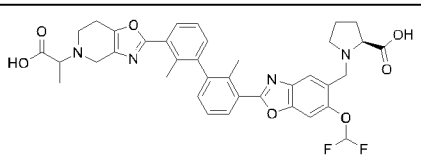
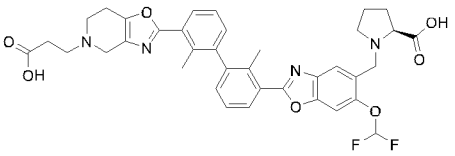
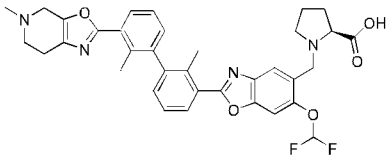
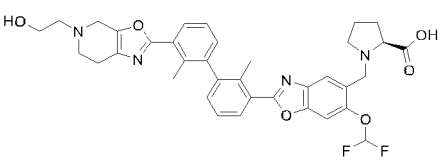
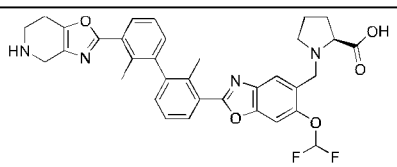
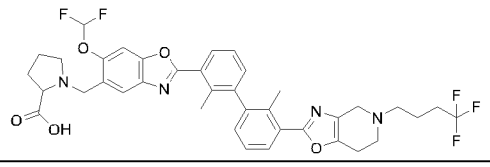


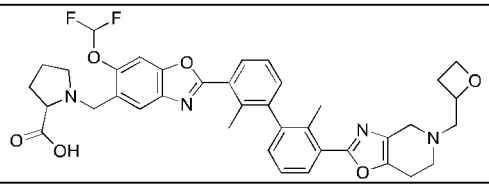
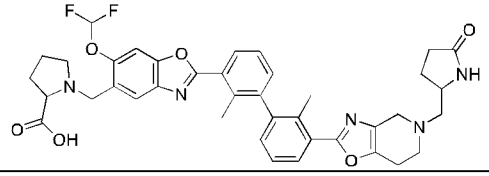
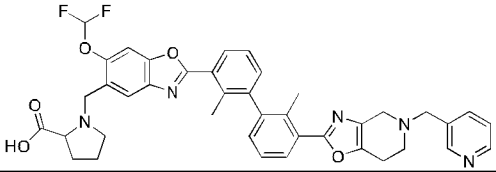
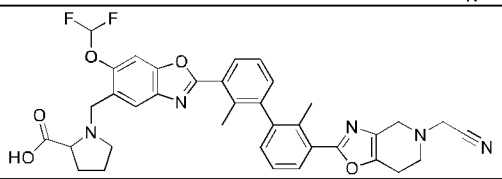
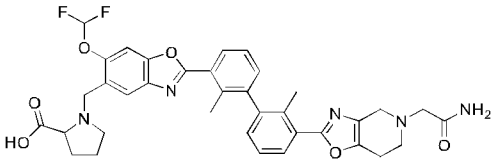
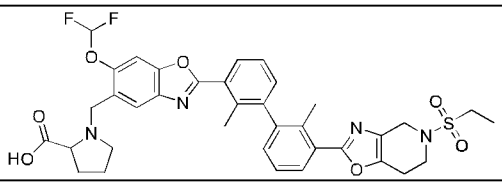
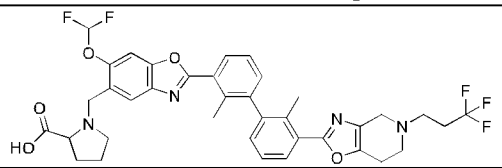
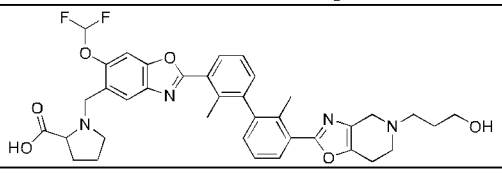
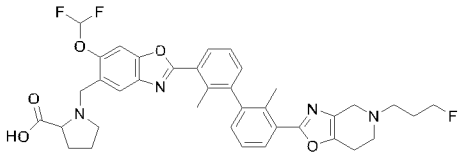
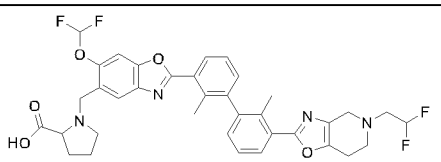
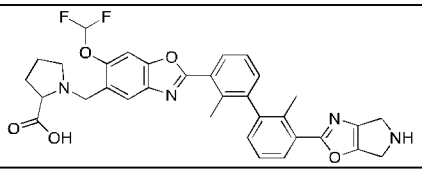
314-9 compound 314

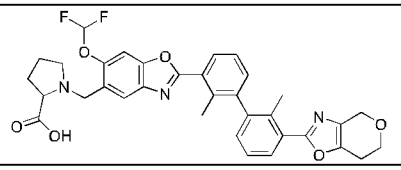
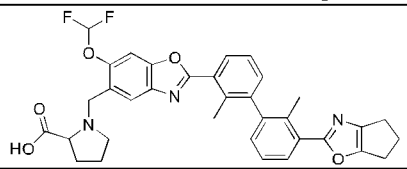
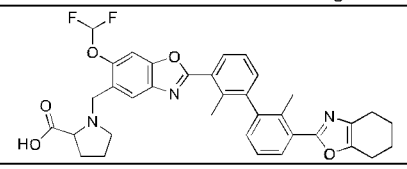
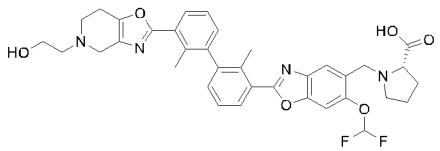
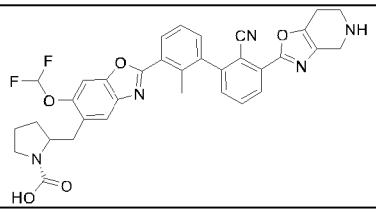
This compound was prepared using similar procedures as described as step 5 in example 1, with compound 314-9 replacing compound 1-4. The crude product was purified by TLC purification (DCM: MeOH = 4: 1) to give 210 mg ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-methyl-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline (compound 314) as off-white solid. LC-MS(m/z):629.3$(M+H)^+$.

The compounds of table 4 were prepared in a similar manner to Examples 314 via different reaction starting materials and suitable reagents.

Table 4

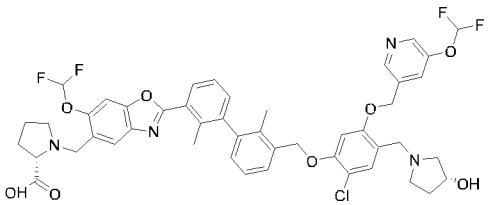
EX No.	Chemical Name	Structure	Physical Data (MS) $(M+H)^+$
184	((2-(3'-(5-(carboxymethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		673.2
185	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(2-(methylsulfonyl)ethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		721.3
186	((2-(3'-(5-(1-carboxyethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		687.3
187	((2-(3'-(5-(2-carboxyethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		687.3
188	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-methyl-4,5,6,7-tetrahydrooxazolo[5,4-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		629.3
189	((6-(difluoromethoxy)-2-(3'-(5-(2-hydroxyethyl)-4,5,6,7-tetrahydrooxazolo[5,4-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		659.3
190	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		615.2
191	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(4,4,4-trifluorobutyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline		725.3

192	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(oxetan-2-ylmethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline		685.3
193	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((5-oxopyrrolidin-2-yl)methyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline		712.3
194	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyridin-3-ylmethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline		706.3
195	((2-(3'-(5-(cyanomethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline		654.2
196	((2-(3'-(5-(2-amino-2-oxoethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline		672.3
197	((6-(difluoromethoxy)-2-(3'-(5-(ethylsulfonyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline		707.2
198	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(3,3,3-trifluoropropyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline		711.2
199	((6-(difluoromethoxy)-2-(3'-(5-(3-hydroxypropyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline		673.3
200	((6-(difluoromethoxy)-2-(3'-(5-(3-fluoropropyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline		675.3
201	((2-(3'-(5-(2,2-difluoroethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline		679.3
202	((6-(difluoromethoxy)-2-(3'-(5,6-dihydro-4H-pyrrolo[3,4-d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline		601.2

203	((6-(difluoromethoxy)-2-(3'-(6,7-dihydro-4H-pyrano[3,4-d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline		616.2
204	((6-(difluoromethoxy)-2-(3'-(5,6-dihydro-4H-cyclopenta[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline		600.2
205	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(4,5,6,7-tetrahydrobenzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline		614.2
206	((6-(difluoromethoxy)-2-(3'-(5-(2-hydroxyethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		659.3
207	2-((2-(2'-cyano-2-methyl-3'-(4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)pyrrolidine-1-carboxylic acid		626.2

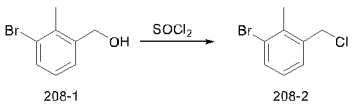
Example 208 Synthesis of compound 208

((2-(3'-((2-chloro-5-((5-(difluoromethoxy)pyridin-3-yl)methoxy)-4-(((R)-3-hydroxypyrrolidin-1-yl)methyl)phenoxy)methyl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline



Compound 208

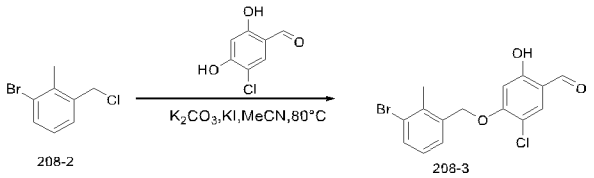
Step 1: Preparation of 1-bromo-3-(chloromethyl)-2-methylbenzene



208-1 208-2

(3-bromo-2-methylphenyl)methanol (20 g) was dissolved in DCM (200 ml), stirred at room temperature, and slowly added 20 ml $SOCl_2$. The mixture was stirred for 2 hrs and then concentrated to give 1-bromo-3-(chloromethyl)-2-methylbenzene (23.1 g).

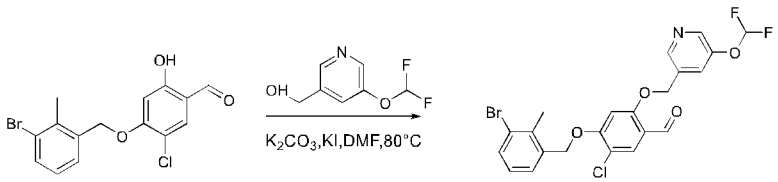
Step 2: Preparation of 4-((3-bromo-2-methylbenzyl)oxy)-5-chloro-2-hydroxybenzaldehyde



208-2 208-3

A mixture of 1-bromo-3-(chloromethyl)-2-methylbenzene (2.0 g), 5-chloro-2,4-dihydroxybenzaldehyde (2.34 g), potassium carbonate (3.78 g), KI (1.51 g) in acetonitrile (20 mL) was stirred at 80 °C overnight. The reaction was completed and added 20 mL water to concentrate, filtered and dried to give 4-((3-bromo-2-methylbenzyl)oxy)-5-chloro-2-hydroxybenzaldehyde (2.8 g).

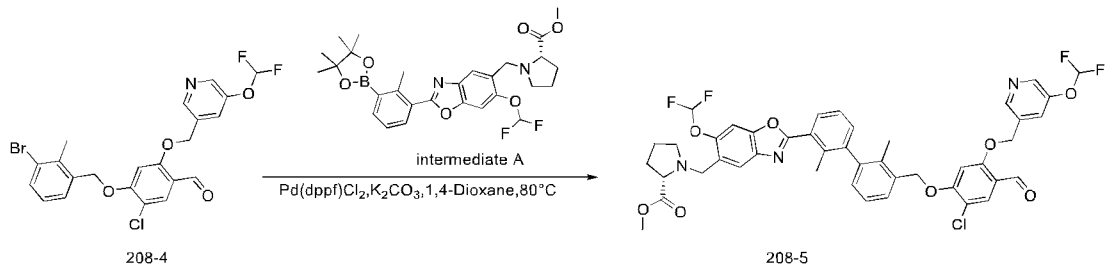
Step 3: Preparation of 4-((3-bromo-2-methylbenzyl)oxy)-5-chloro-2-((5-(difluoromethoxy)pyridin-3-yl)methoxy)benzaldehyde



208-3 208-4

Compound 208-3 (500 mg), (5-(difluoromethoxy)pyridin-3-yl)methanol (408 mg), potassium carbonate (585 mg), KI (195 mg) was added to acetonitrile (10 mL), the reaction mixture was stirred at 80 °C overnight. 10 mL water was added, the mixture was concentrated, filtered and dried to give 4-((3-bromo-2-methylbenzyl) oxy)-5-chloro-2-((5-(difluoromethoxy) pyridin-3-yl) methoxy) benzaldehyde (478 mg).

Step 4: Preparation of methyl ((2-(3'-((2-chloro-5-((5-(difluoromethoxy)pyridin-3-yl)methoxy)-4-formylphenoxy)methyl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-prolinate

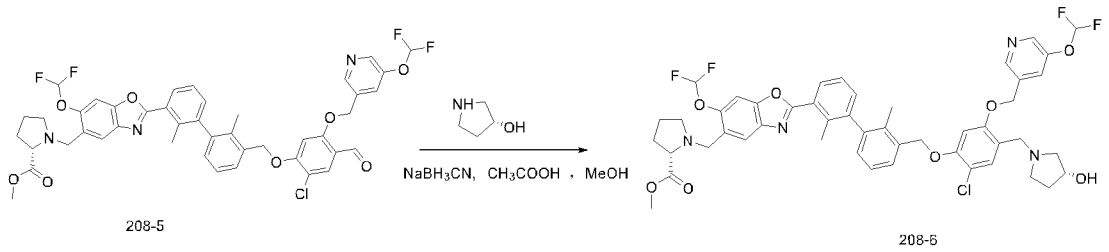


208-4 208-5

Compound 208-4 (470 mg), intermediate A (597 mg)and potassium carbonate (236 mg) were added to 1,4-dioxane(12 mL) and water(3 mL) with stirring, and then $Pd(dppf)Cl_2$ was added to the mixture under N_2 atmosphere. The reaction mixture was heated to 80 °C and stirred overnight. The mixture was quenched with water (30mL) and extract with DCM (30 mL×3). The

organic layers were dried over anhydrous sodium sulfate, filter, concentrate and purified by column (DCM/MeOH: 15/1) to obtain compound 208-5 (550 mg).

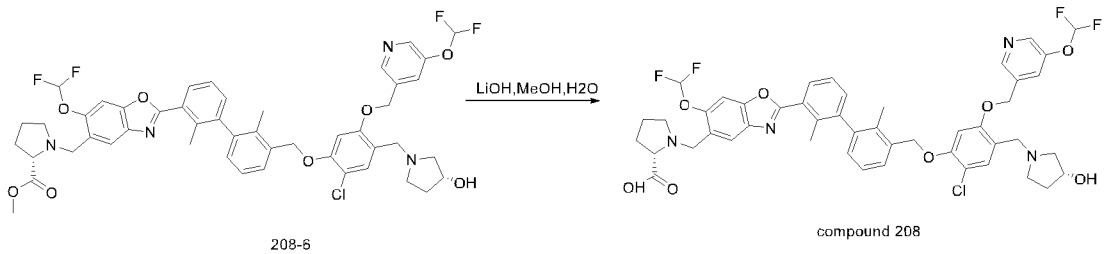
Step 5: Preparation of methyl ((2-(3'-((2-chloro-5-((5-(difluoromethoxy)pyridin-3-yl)methoxy)-4-(((R)-3-hydroxypyrrolidin-1-yl)methyl)phenoxy)methyl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-prolinate



208-5 208-6

Compound 208-5 (270 mg), (R)-pyrrolidin-3-ol (80 mg), glacial acetic acid (40 mg) were added to 10 mL methanol with stirring, the mixture was heated to 50 °C and stirred for 1 h. After the mixture was cooled to room temperature, sodium cyanoborohydride was added and the mixture was stirred at room temperature for 2 hrs. Then the mixture was diluted with water(10mL) and extract with DCM (15 mL×3), the organic layers were dried over anhydrous sodium sulfate, filtered, concentrated and purified by column (DCM/MeOH=15/1) to obtain compound 208-6 (110 mg).

Step 6: Preparation of ((2-(3'-((2-chloro-5-((5-(difluoromethoxy)pyridin-3-yl)methoxy)-4-(((R)-3-hydroxypyrrolidin-1-yl)methyl)phenoxy)methyl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline(compound 208)

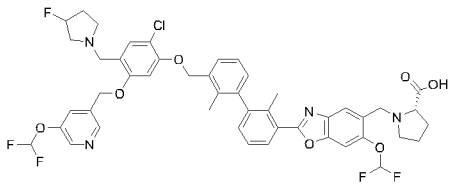
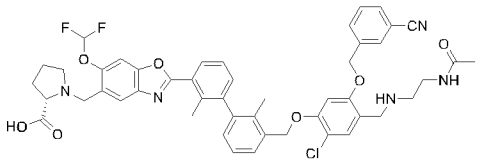
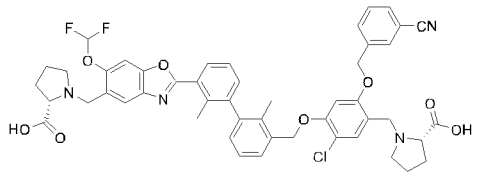
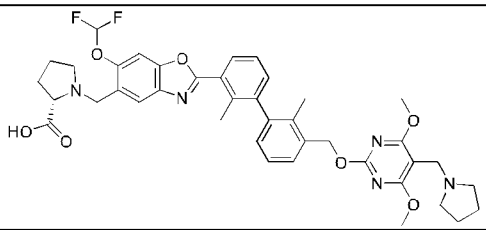
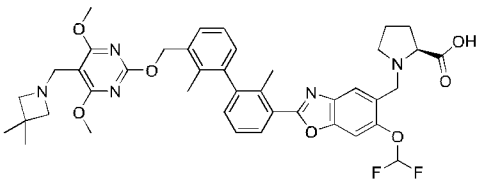
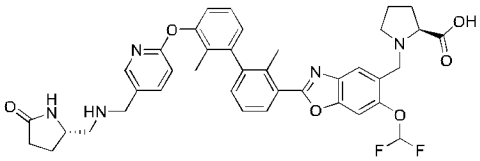


208-6 compound 208

Compound 208-6 (110 mg) was added to 5 mL methanol under stirring, and 8 mg LiOH was weighed and dissolved in 1 mL water, and then added to the mixture, the reaction mixture was heated to 35 °C overnight. The mixture was added with 10 mL water and extracted with DCM (15 mL×3). The organic layers were dried over anhydrous sodium sulfate, filtered and concentrated to give 105 mg ((2-(3'-((2-chloro-5-((5-(difluoromethoxy)pyridin-3-yl)methoxy)-4-(((R)-3-hydroxypyrrolidin-1-yl)methyl)phenoxy)methyl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline (compound 208). LC-MS(m/z):905.3$(M+H)^+$.

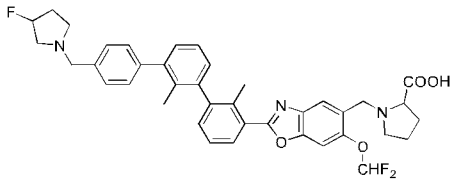
The compounds of table 5 were prepared in a similar manner to Example 208 via different reaction starting materials and suitable reagents.

Table 5

EX No.	Chemical Name	Structure	Physical Data (MS) $(M+H)^+$
209	((2-(3'-((2-chloro-5-((5-(difluoromethoxy)pyridin-3-yl)methoxy)-4-((3-fluoropyrrolidin-1-yl)methyl)phenoxy)methyl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		907.3
210	((2-(3'-((4-(((2-acetamidoethyl)amino)methyl)-2-chloro-5-((3-cyanobenzyl)oxy)phenoxy)methyl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		878.3
211	((2-(3'-((4-(((S)-2-carboxypyrrolidin-1-yl)methyl)-2-chloro-5-((3-cyanobenzyl)oxy)phenoxy)methyl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		891.3
212	((6-(difluoromethoxy)-2-(3'-(((4,6-dimethoxy-5-(pyrrolidin-1-ylmethyl)pyrimidin-2-yl)oxy)methyl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		744.3
213	((6-(difluoromethoxy)-2-(3'-(((5-((3,3-dimethylazetidin-1-yl)methyl)-4,6-dimethoxypyrimidin-2-yl)oxy)methyl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		758.3
214	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-((5-(((((S)-5-oxopyrrolidin-2-yl)methyl)amino)methyl)pyridin-2-yl)oxy)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		712.3

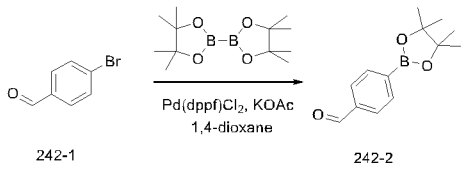
Example 242 Synthesis of compound 242

((6-(difluoromethoxy)-2-(4''-((3-fluoropyrrolidin-1-yl)methyl)-2,2'-dimethyl-[1,1':3',1''-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline



Compound 242

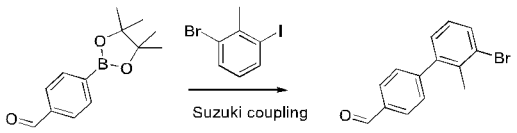
Step 1: Preparation of 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde



242-1 242-2

To a solution of 4-bromobenzaldehyde (9.25 g) in 1,4-dioxane (120 mL) was added Bis(pinacolato)diboron (15.8 g), Pd(dppf)Cl_2.DCM (0.48 g) and KOAc (20.0 g). The reaction mixture was heated at 100 °C for 4 hrs. The mixture was diluted with 150 mL of water and then extracted with EtOAc (150 mL×2). The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was was purified by silicagel (eluting with hexane-EtOAc using a gradient from 20:1 to 10:1) to afford 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde (11.2 g) as white solid.

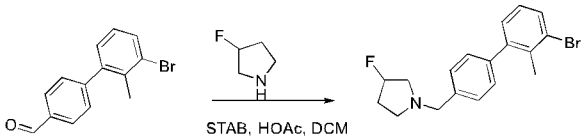
Step 2: Preparation of 3'-bromo-2'-methyl-[1,1'-biphenyl]-4-carbaldehyde



242-2 242-3

To a solution of compound 242-2 (60 mL) in EtOH (20 mL), was added 10% Na_2CO_3 aq. (20 mL) and Pd(dppf)Cl_2.DCM (420 mg), and then 1-bromo-3-iodo-2-methylbenzene (9.0 g) was added dropwise under N_2 protection. The mixture was stirred at 100 °C for 16 hrs. The reaction was quenched with H_2O (50 mL) and extracted with EtOAc (100 mL) for 3 times. The organic layers were combined and washed with brine. The resulting solution was concentrated and purified by silicagel (eluting with hexane-EtOAc using a gradient from 20:1 to 10:1) to afford 3'-bromo-2'-methyl-[1,1'-biphenyl]-4-carbaldehyde (3.2 g) as a light yellow solid.

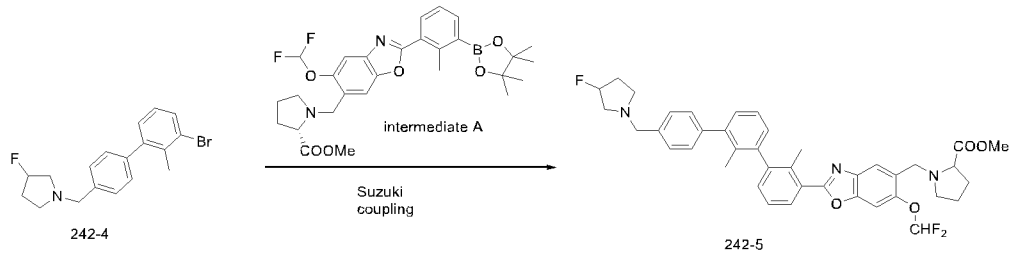
Step 3: Preparation of 1-((3'-bromo-2'-methyl-[1,1'-biphenyl]-4-yl)methyl)-3-fluoropyrrolidine



242-3 242-4

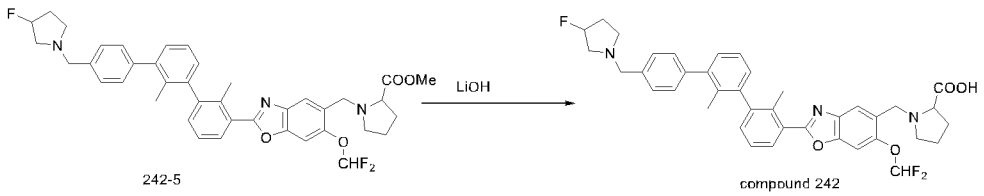
3'-bromo-2'-methyl-[1,1'-biphenyl]-4-carbaldehyde (275 mg) was dissolved in 5 mL DCM. 3-fluoropyrrolidine (120 mg) and HOAC was added in one portion. The resulting mixture was stirred for 1 h at room temperature then STAB (420 mg) was added in one portion at the same temperature. The reaction was allowed to stir at room temperature for 3 h. The resulting mixture was quenched with saturated Na_2CO_3 and extracted with EtOAc (20 mL) for 3 times and the organic phase was dried over Na_2SO_4. The resulting solution was concentrated to afford 1-((3'-bromo-2'-methyl-[1,1'-biphenyl]-4-yl)methyl)-3-fluoropyrrolidine (320 mg) as a colorless oil.

Step 4: Preparation of methyl ((6-(difluoromethoxy)-2-(4''-((3-fluoropyrrolidin-1-yl)methyl)-2,2'-dimethyl-[1,1':3',1''-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)prolinate



This compound was prepared using similar procedures as described as step 4 in example 171, with compound 242-4 replacing compound 171-4. The resulting mixture was purified by RP-column (mobile phase: MeCN: water (0.1% HCl) using a gradient from 40:60 to 50:50) to afford compound 242-5 (288 mg).

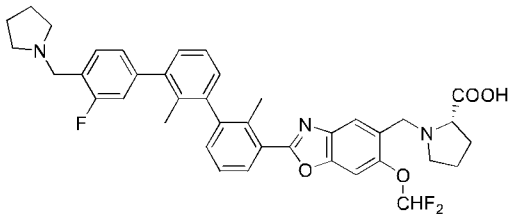
Step 5: Preparation of ((6-(difluoromethoxy)-2-(4''-((3-fluoropyrrolidin-1-yl)methyl)-2,2'-dimethyl-[1,1':3',1''-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline



This compound was prepared using similar procedures as described as step 6 in example 171, with compound 242-5 replacing compound 171-6. The crude product was purified by RP-column (mobile phase: MeCN : water (0.1% HCl) using a gradient from 40:60 to 50:50) to afford methyl ((6-(difluoromethoxy)-2-(4''-((3-fluoropyrrolidin-1-yl)methyl)-2,2'-dimethyl-[1,1':3',1''-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)prolinate as a white solid (168 mg) (compoud 242). LC-MS(m/z):670.3$(M+H)^+$.

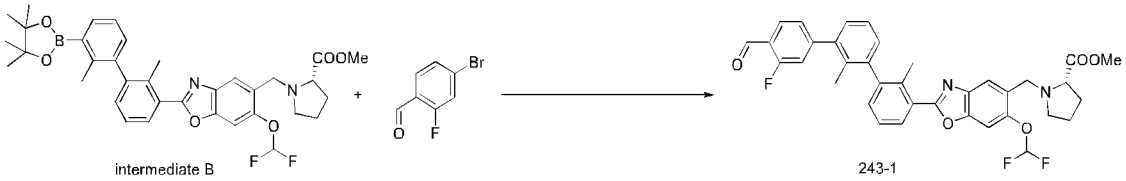
Example 243 Synthesis of compound 243

((6-(difluoromethoxy)-2-(4''-((3-fluoropyrrolidin-1-yl)methyl)-2,2'-dimethyl-[1,1':3',1''-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline



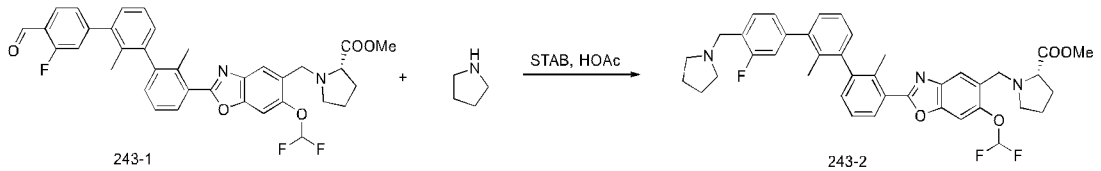
Compound 243

Step 1: Preparation of methyl ((6-(difluoromethoxy)-2-(3''-fluoro-4''-formyl-2,2'-dimethyl-[1,1':3',1''-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-prolinate



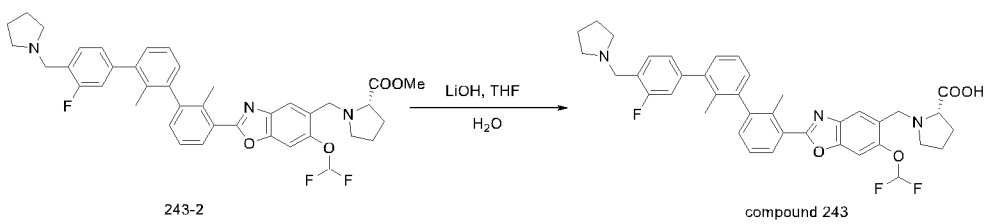
This compound was prepared using similar procedures as described as step 1 in example 1, with 4-bromo-2-fluorobenzaldehyde replacing compound a-6, and with intermediate B replacing intermediate A. The resulting solution was concentrated and purified by silicagel (eluting with Hexane-EtOAc using a gradient from 5:1) to afford the tiltle compound as a yellow oil.

Step 2: Preparation of methyl ((6-(difluoromethoxy)-2-(4''-((3-fluoropyrrolidin-1-yl)methyl)-2,2'-dimethyl-[1,1':3',1''-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)prolinate



This compound was prepared using similar procedures as described as step 5 in example 2, with compound 243-1 replacing compound 2-4, and with pyrrolidine replacing L-proline. The resulting solution was concentrated to afford the tilte compound as a colorless oil.

Step 5: Preparation of ((6-(difluoromethoxy)-2-(3''-fluoro-2,2'-dimethyl-4''-(pyrrolidin-1-ylmethyl)-[1,1':3',1''-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline

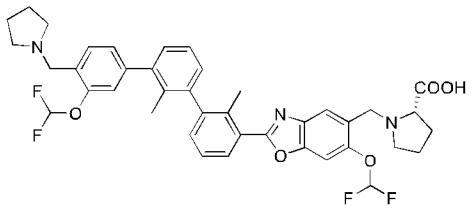


This compound was prepared using similar procedures as described as step 5 in example 1, with compound 243-2 replacing compound 1-4. The crude product was purified by RP-column (mobile phase: MeCN : water (0.1% HCl) using a gradient from 10:90 to 30:70) to afford the tilte compound. LC-MS(m/z):670.3$(M+H)^+$. ^{1}H NMR (500 MHz, Methanol-d4) δ: 8.16 (dd, 1H, J = 7.9, 1.5 Hz), 8.07 (s, 1H), 7.76 (s, 1H), 7.70 (t, 1H, J = 7.7 Hz), 7.50 (t, 1H, *J* = 7.7 Hz), 7.43–

7.27 (m, 5H), 7.20 (dd, 1H , J = 7.5, 1.4 Hz), 7.12 (t, 1H, J_{F-H}= 72.6 Hz), 4.75 (d, 1H, J = 13.1 Hz), 4.54 (d, 1H, J = 13.1 Hz), 4.54 (s, 2H), 4.37 (dd, 1H, J = 9.5, 7.4 Hz), 3.66-3.60 (m, 3H), 3.45-3.40 (m, 1H), 3.29-3.23 (m, 2H), 2.65-2.57 (m, 1H), 2.49 (s, 3H), 2.28–2.14 (m, 4H), 2.10-2.00 (m, 3H), 1.96 (s, 3H).

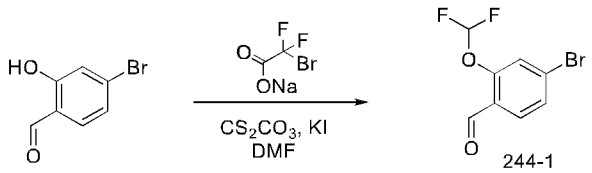
Example 244 Synthesis of compound 244

((6-(difluoromethoxy)-2-(3''-(difluoromethoxy)-2,2'-dimethyl-4''-(pyrrolidin-1-ylmethyl)-[1,1':3',1''-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline



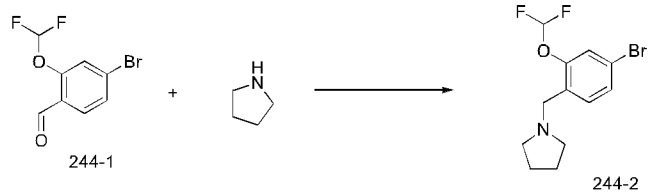
Compound 244

Step 1: Preparation of 4-bromo-2-(difluoromethoxy)benzaldehyde



To a solution of 4-bromo-2-hydroxybenzaldehyde (4.0g) in DMF (50 mL), Cs_2CO_3 (9.8 g), KI (400 mg) was added. The mixture was stirred at room temperature for 30 mins, and then sodium 2-bromo-2,2-difluoroacetate (6.0 g) was added in small portions. The mixture was stirred at 75 °C overnight. The mixture was diluted with 100 mL of water and then extracted with EtOAc (100 ml) for three times. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by silicagel (eluting with hexane-EtOAc using a gradient from 8:1 to 5:1) to afford 4-bromo-2-(difluoromethoxy)benzaldehyde (2.8 g) as a brown oil.

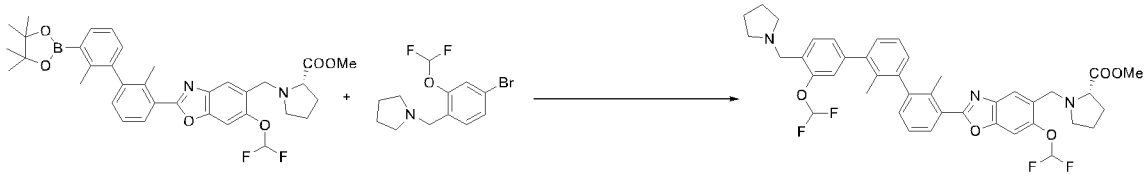
Step 2: Preparation of 5-bromo-2-(pyrrolidin-1-ylmethyl)benzonitrile



This compound was prepared using similar procedures as described as step 5 in example 2, with compound 244-1 replacing compound 2-4, and with pyrrolidine replacing L-proline. The

cude product was purified by silicagel (eluting with DCM-MeOH using a gradient from 20:1 to 10:1) to afford the title compound.

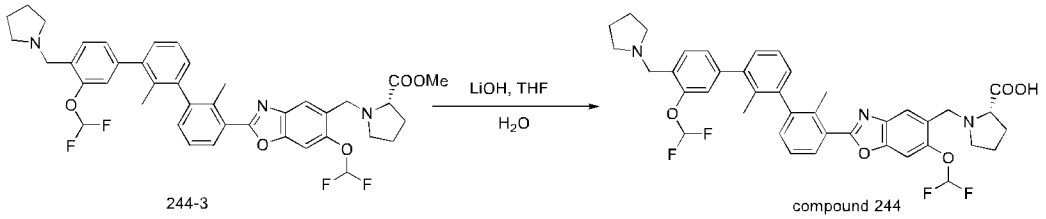
Step 3: Preparation of methyl ((6-(difluoromethoxy)-2-(3''-(difluoromethoxy)-2,2'-dimethyl-4''-(pyrrolidin-1-ylmethyl)-[1,1':3',1''-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-prolinate



intermediate B 244-2 244-3

This compound was prepared using similar procedures as described as step 1 in example 1, with compound 244-2 replacing compound a-6, and with intermediate B replacing intermediate A. The resulting solution was concentrated and purified by silicagel (eluting with Hexane-EtOAc using a gradient from 5:1 to 1:1) to get the tilte compound.

Step 4: Preparation of ((6-(difluoromethoxy)-2-(3''-(difluoromethoxy)-2,2'-dimethyl-4''-(pyrrolidin-1-ylmethyl)-[1,1':3',1''-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline

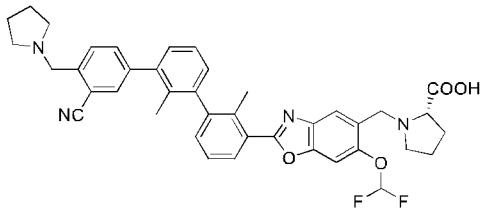


244-3 compound 244

This compound was prepared using similar procedures as described as step 5 in example 1, with compound 244-3 replacing compound 1-4.The crude product was purified by RP-column (mobile phase: MeCN : water (0.1% HCl) using a gradient from 10:90 to 35:65) to afford the title compound. LC-MS(m/z):718.3$(M+H)^+$. ^{1}H NMR (500 MHz, Methanol-d4), δ: 8.16 (dd, 1H, J = 7.9, 1.5 Hz), 8.07 (s, 1H), 7.76 (s, 1H), 7.73 (d, 1H, J = 7.9 Hz), 7.50 (t, 1H, J = 7.7 Hz), 7.42–7.36 (m, 3H), 7.34 (d, 1H, J =1.4 Hz), 7.30 (dd, 1H, J = 7.7, 1.4 Hz), 7.21 (dd, 1H, J = 7.4, 1.4 Hz), 7.13 (td, 2H, J = 72.8, 2.4 Hz), 4.73 (d, 1H, J=13.2 Hz), 4.61 (d, 1H, J = 13.2 Hz), 4.53 (s, 2H), 4.30 (dd, 1H, J = 9.7, 7.1 Hz), 3.69–3.56 (m, 3H), 3.44-3.38 (m, 1H), 3.31-3.28 (m,2H), 2.62-2.55 (m, 1H), 2.50 (s, 3H), 2.23-2.15 (m, 4H), 2.12–2.00 (m, 3H), 1.96 (s, 3H)

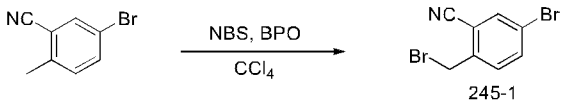
Example 245 Synthesis of compound 245

((2-(3''-cyano-2,2'-dimethyl-4''-(pyrrolidin-1-ylmethyl)-[1,1':3',1''-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline



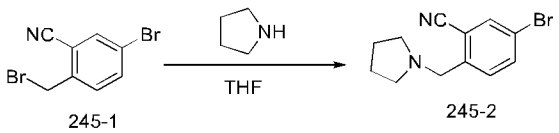
Compound 245

Step 1: Preparation of 5-bromo-2-(bromomethyl)benzonitrile



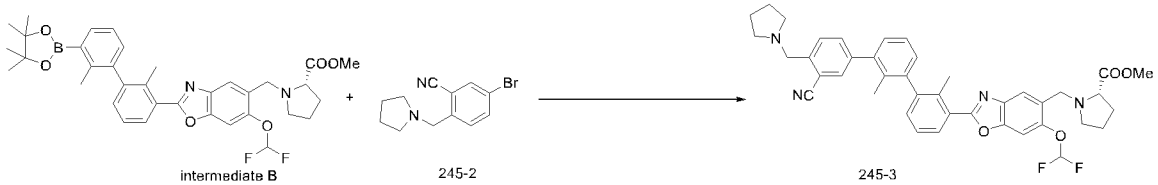
To a solution of 5-bromo-2-methylbenzonitrile (20.0 g), NBS (19.6 g) in CCl_4 (300 mL) was added BPO (2.4 g) under N_2 protection. The mixture was allowed to stir at 70 °C overnight. The reaction was quenched with saturated $NaHCO_3$ solution (200 mL). The organic layers were combined and washed with brine. The resulting solution was concentrated and purified by silicagel (eluting with Hexane-EtOAc using a gradient from 20:1 to 1:1) to afford 5-bromo-2-(bromomethyl)benzonitrile (15.2 g) as a yellow solid crude product.

Step 2: Preparation of 5-bromo-2-(pyrrolidin-1-ylmethyl)benzonitrile



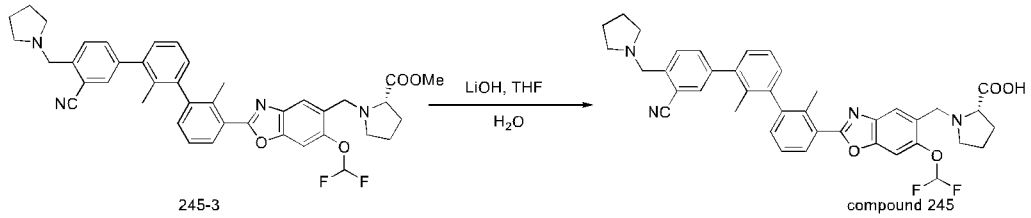
To a solution of compound 245-1 (5.4 g) in THF (60 mL) was added Pyrrolidine (2.85 g) added dropwise under 0 °C. The reaction mixture was heated to 40 °C for 5 hrs. The reaction mixture was diluted with 200 mL of water and then extracted with EtOAc (150 ml) for three times. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by silicagel (eluting with hexane-EtOAc using a gradient from 2:1 to 1:2) to afford 5-bromo-2-(pyrrolidin-1-ylmethyl)benzonitrile (3.8 g) as a brown oil.

Step 3: Preparation of methyl ((2-(3''-cyano-2,2'-dimethyl-4''-(pyrrolidin-1-ylmethyl)-[1,1':3',1''-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-prolinate



This compound was prepared using similar procedures as described as step 1 in example 1, with compound 245-2 replacing compound a-6, and with intermediate B replacing intermediate A. The crude product purified by silicagel (eluting with Hexane-EtOAc using a gradient from 5:1 to 1:1) to get the tilte compound.

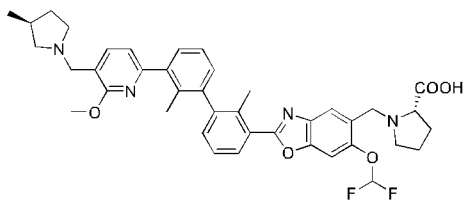
Step 4: Preparation of ((2-(3''-cyano-2,2'-dimethyl-4''-(pyrrolidin-1-ylmethyl)-[1,1':3',1''-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline



This compound was prepared using similar procedures as described as step 5 in example 1, with compound 245-3 replacing compound 1-4. The crude product was purified by RP-column (mobile phase: MeCN : water (0.1% HCl) using a gradient from 10:90 to 35:65) to get the title compound. LC-MS(m/z):677.3$(M+H)^+$. ^{1}H NMR (500 MHz, Methanol-d4) δ: 8.21 (dd, 1H, J = 7.9, 1.5 Hz), 8.10 (s, 1H), 7.76 (s, 1H), 7.70 (t, 1H, J = 7.7 Hz), 7.50 (t, 1H, J = 7.7 Hz), 7.49-7.28 (m, 5H), 7.20 (dd, 1H , J = 7.5, 1.4 Hz), 7.12 (t, 1H, J_{F-H}= 72.6 Hz), 4.73 (d, 1H, J = 13.1 Hz), 4.51 (d, 1H, J = 13.1 Hz), 4.51 (s, 2H), 4.37 (dd, 1H, J = 9.5, 7.4 Hz), 3.69-3.51 (m, 3H), 3.47-3.42 (m, 1H), 3.25-3.20 (m, 2H), 2.65-2.57 (m, 1H), 2.49 (s, 3H), 2.28-2.12 (m, 4H), 2.10-2.00 (m, 3H), 1.96 (s, 3H).

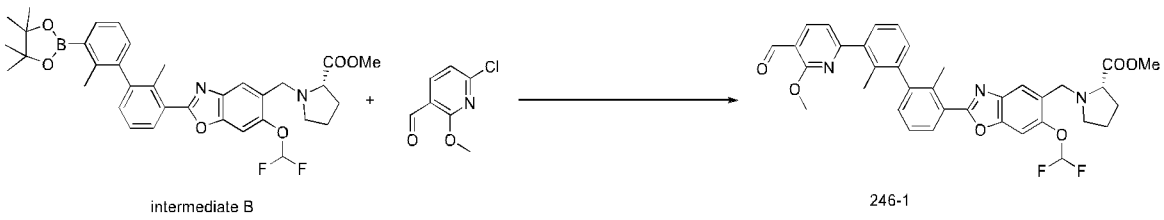
Example 246 Synthesis of compound 246

((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(((S)-3-methylpyrrolidin-1-yl)methyl)pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline



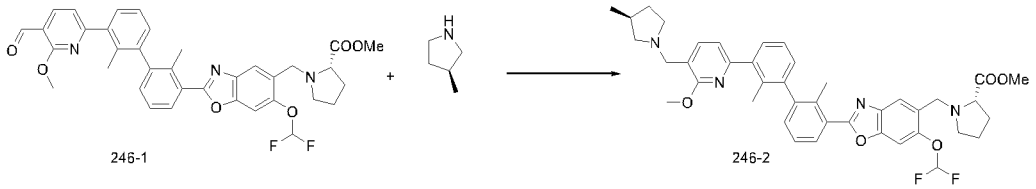
Compound 246

Step 1: Preparation of methyl ((6-(difluoromethoxy)-2-(3'-(5-formyl-6-methoxypyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-prolinate



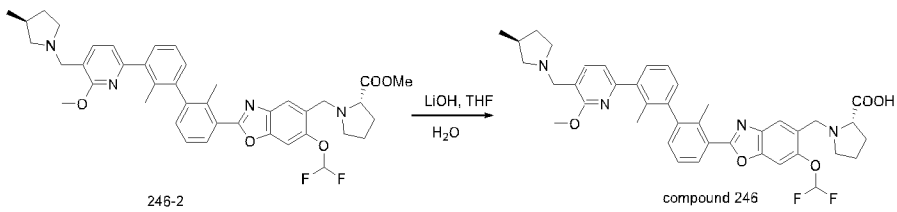
This compound was prepared using similar procedures as described as step 1 in example 1, with 6-chloro-2-methoxynicotinaldehyde replacing compound a-6, and with intermediate B replacing intermediate A. The crude product was purified by silicagel (Hexane-EtOAc = 3:1) to get the titled compound.

Step 2: Methyl ((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(((S)-3-methylpyrrolidin-1-yl)methyl)pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-prolinate



This compound was prepared using similar procedures as described as step 5 in example 2, with compound 246-1 replacing compound 2-4, and with (S)-3-methylpyrrolidine replacing L-proline. The resulting solution was concentrated to afford the tilte compound.

Step 3: ((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(((S)-3-methylpyrrolidin-1-yl)methyl)pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline

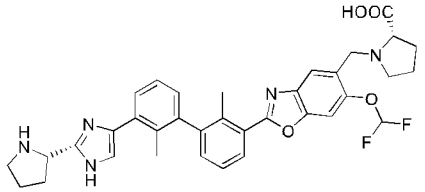


This compound was prepared using similar procedures as described as step 5 in example 1, with compound 246-2 replacing compound 1-4. The orgainic layer was separated and purified by RP-column (mobile phase: MeCN : water (0.1% HCl) using a gradient from 15:85 to 30:70) to afford ((6-(difluoromethoxy)-2-(3"-(difluoromethoxy)-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline (30.8 mg) as a white solid. LC-MS(m/z):697.3$(M+H)^+$. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.11 (dd, 1H, J = 7.9, 1.5 Hz), 7.96 (s, 1H), 7.77 (d, 1H, J = 7.5 Hz), 7.72 (s, 1H), 7.54-7.37 (m,5H), 7.24-7.19 (m, 1H), 7.16 (d, 1H, J = 7.5 Hz), 3.95 (s, 2H), 3.89 (s, 3H), 3.58 (s, 2H), 3.11-3.03 (m, 1H), 2.78 (t, 1H, J = 2.8 Hz), 2.68–2.60 (m, 1H), 2.60-2.52 (m, 3H), 2.45 (s, 3H), 2.22-2.16 (m, 1H), 2.15-

2.07 (m, 2H), 2.05 (s, 3H), 2.02-1.93 (m, 1H), 1.88-1.70 (m, 3H), 1.34-1.27 (m, 1H), 1.00 (d, *J* = 6.7 Hz, 3H).

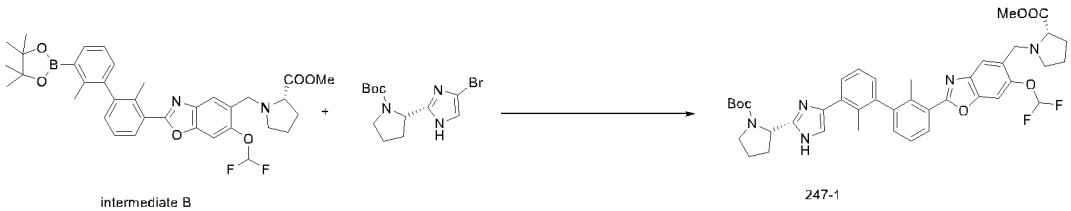
Example 247 Synthesis of compound 247

((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(2-((S)-pyrrolidin-2-yl)-1H-imidazol-4-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline



Compound 247

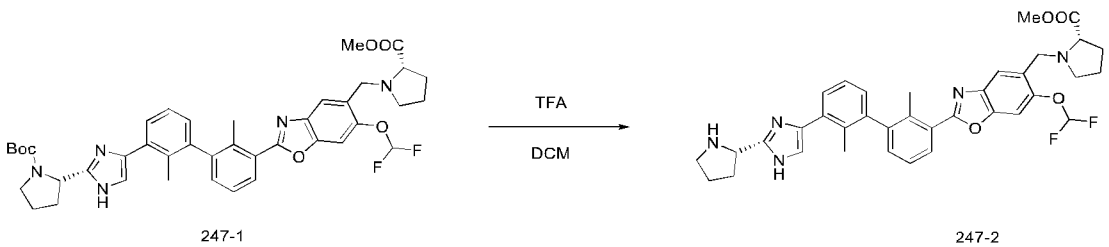
Step 1: Preparation of tert-butyl (S)-2-(4-(3'-(6-(difluoromethoxy)-5-(((S)-2-(methoxycarbonyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-1H-imidazol-2-yl)pyrrolidine-1-carboxylate



intermediate B 247-1

This compound was prepared using similar procedures as described as step 1 in example 1, with tert-butyl (S)-2-(4-bromo-1H-imidazol-2-yl)pyrrolidine-1-carboxylate replacing compound a-6, and with intermediate B replacing intermediate A. The resulting solution was concentrated and purified by silicagel (eluting with Hexane-EtOAc using a gradient from 5:1 to 1:1) to afford tert-butyl (S)-2-(4-(3'-(6-(difluoromethoxy)-5-(((S)-2-(methoxycarbonyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-1H-imidazol-2-yl)pyrrolidine-1-carboxylate (98 mg) as a yellow oil.

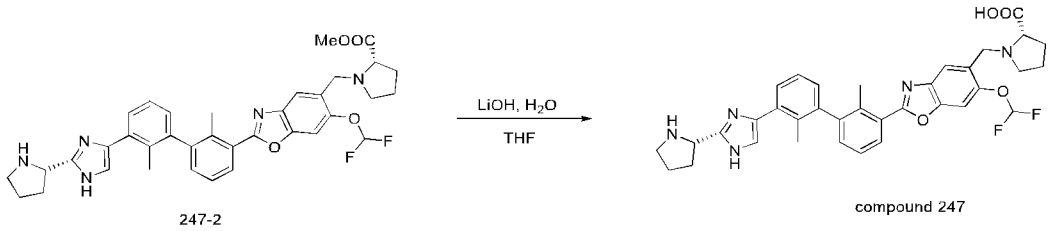
Step 2: Preparation of methyl ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(2-((S)-pyrrolidin-2-yl)-1H-imidazol-4-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-prolinate



247-1 247-2

A mixture of compound 247-1 (76.0 mg) in DCM/TFA = 7:1 (4 mL) was stirred for 4 hrs at room temperature. The resulting solution was concentrated under high vacuum to afford compound 247-2(60 mg) as a yellow semi-solid.

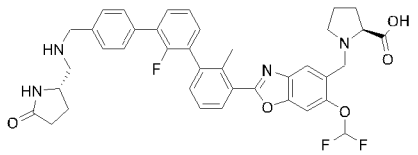
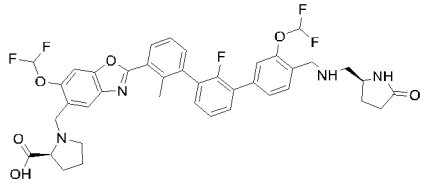
Step 3: Preparation of ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(2-((S)-pyrrolidin-2-yl)-1H-imidazol-4-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline

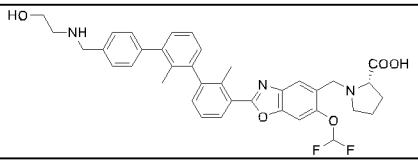
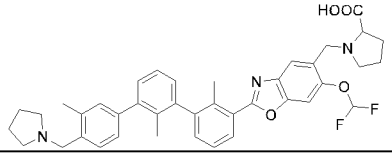
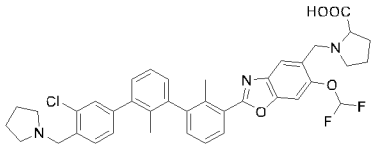
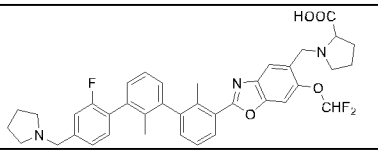
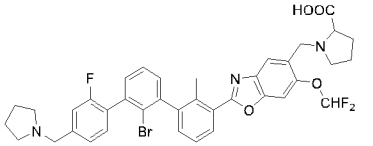
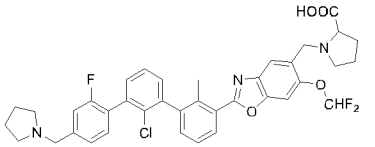
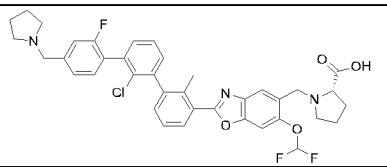
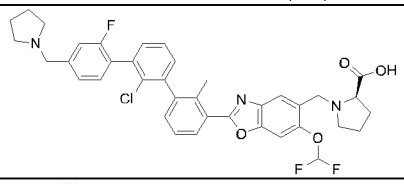
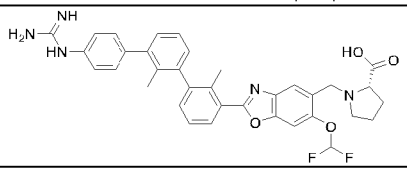
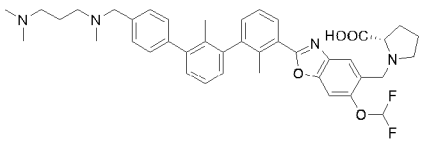
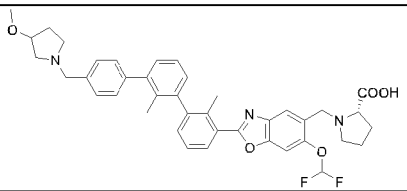


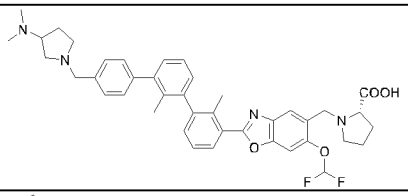
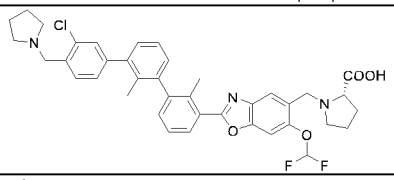
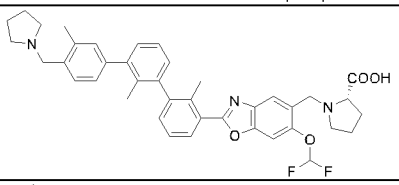
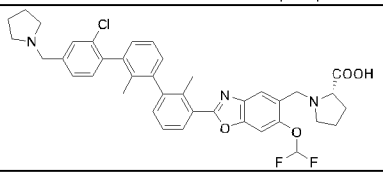
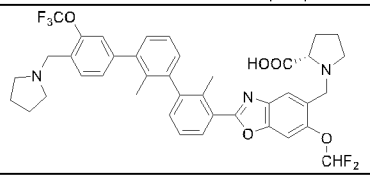
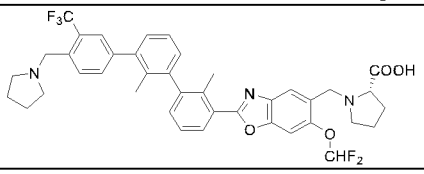
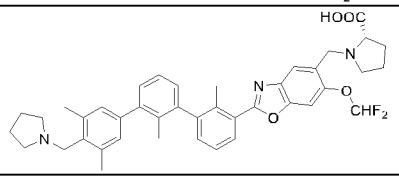
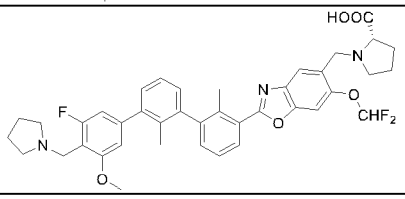
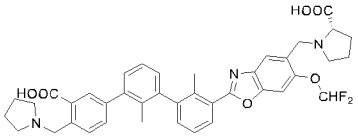
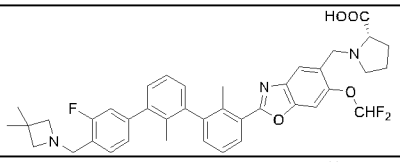
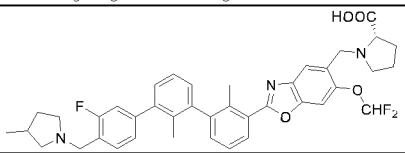
This compound was prepared using similar procedures as described as step 5 in example 1, with compound 247-2 replacing compound 1-4. The crude product was purified by RP-column (mobile phase: MeCN : water (0.1% HCl) using a gradient from 10:90 to 35:65) to afford ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(2-((S)-pyrrolidin-2-yl)-1H-imidazol-4-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline (70.6 mg) as a white solid. LC-MS(m/z):628.3(M+H)$^+$. ^{1}H NMR (500 MHz, Methanol-d4), *δ:* 8.19 (dd, 1H, *J* = 8.0, 1.5 Hz), 8.07 (s, 1H) , 7.76 (d, 1H, *J* = 10.8 Hz), 7.61 (dd, 1H, J = 7.8, 1.3 Hz), 7.52 (t, 1H, *J* = 7.8 Hz), 7.46 (t, 1H, *J* = 7.6 Hz), 7.38 (dd, 1H, *J* = 7.6, 1.4 Hz), 7.32 (dd, 1H, *J* = 7.6, 1.4 Hz), 7.13 (t, 1H, J_{F-H} = 72.6 Hz), 5.16 (t, 1H, *J* = 9.3, 7.7 Hz), 4.79 (d, 1H, *J* = 13.2), 4.62 (d, 1H, *J* = 13.3), 4.48 (t, 1H, *J* = 9.3 Hz), 3.67-3.55 (m, 3H), 3.50-3.42 (m, 1H), 2.75- 2.60 (m, 2H), 2.58-2.50 (m, 1H), 2.49 (s, 3H) , 2.43-2.34 (m, 1H), 2.29 -2.17 (m, 3H), 2.15 (s, 3H) , 2.11-1.99 (m, 1H).

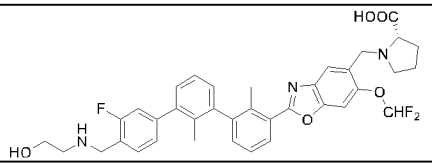
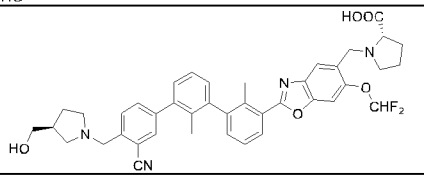
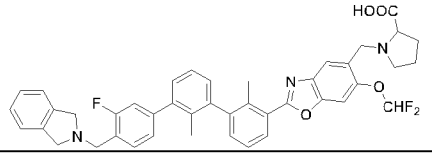
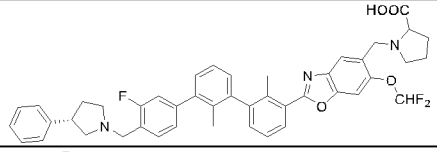
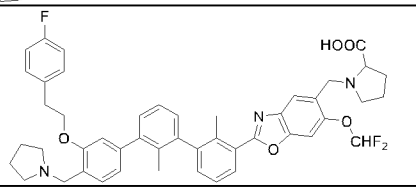
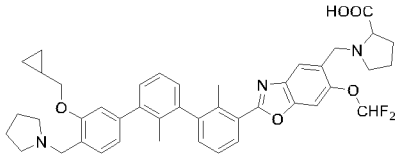
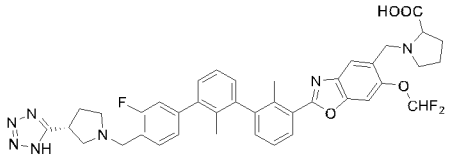
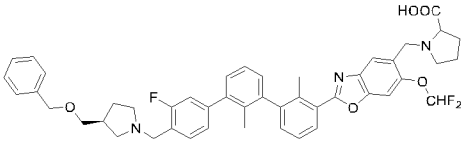
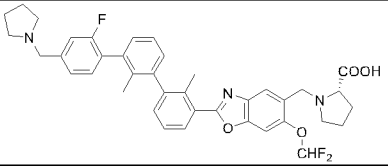
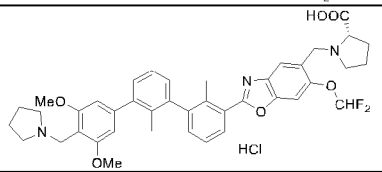
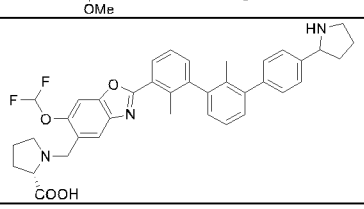
The compounds of table 6 were prepared in a similar manner to Examples 242-247 via different reaction starting materials and suitable reagents.

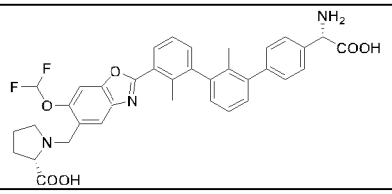
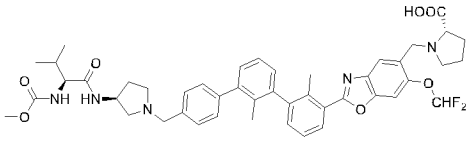
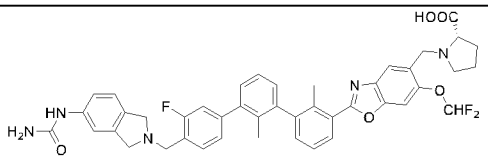
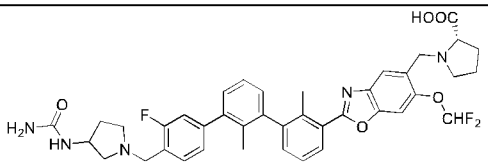
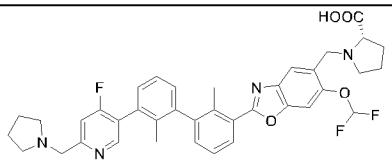
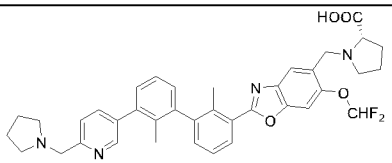
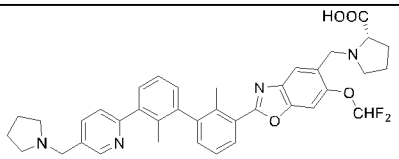
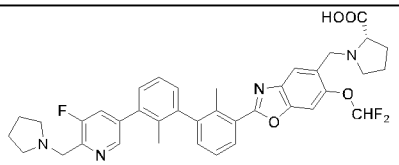
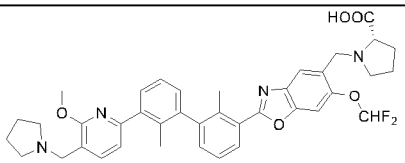
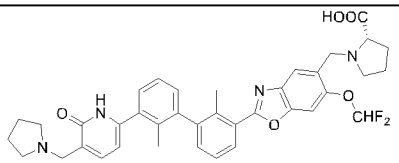
Table 6

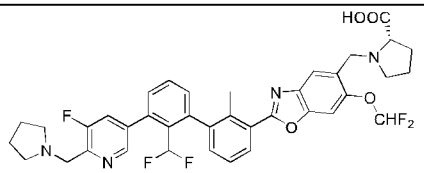
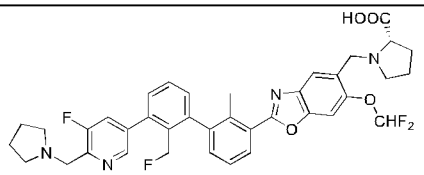
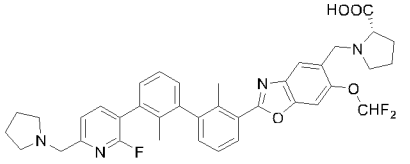
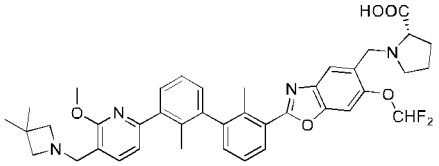
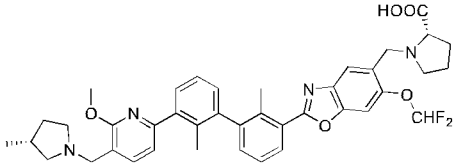
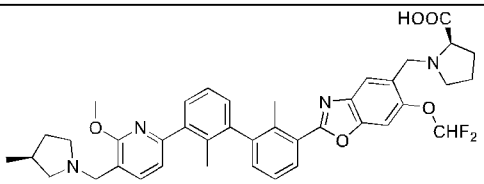
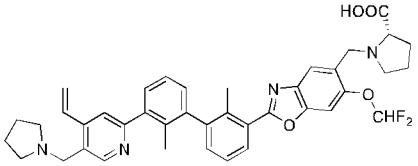
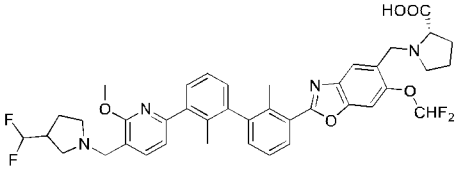
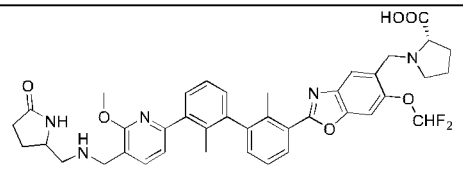
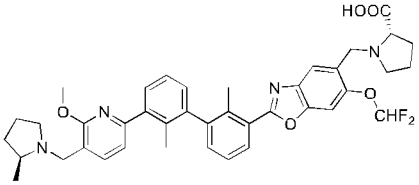
EX No.	Chemical Name	Structure	Physical Data (MS) (M+H)$^+$
215	((6-(difluoromethoxy)-2-(2'-fluoro-2-methyl-4"-(((((S)-5-oxopyrrolidin-2-yl)methyl)amino)methyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		699.3
216	((6-(difluoromethoxy)-2-(3"-(difluoromethoxy)-2'-fluoro-2-methyl-4"-(((((S)-5-oxopyrrolidin-2-yl)methyl)amino)methyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		765.3

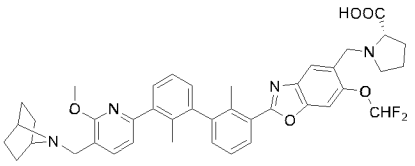
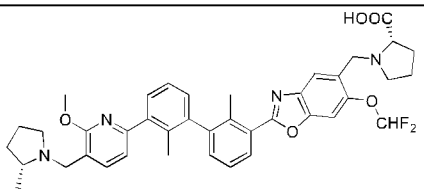
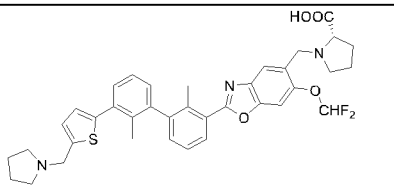
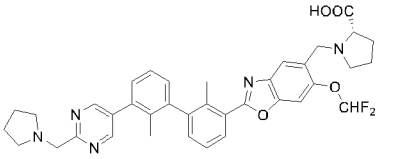
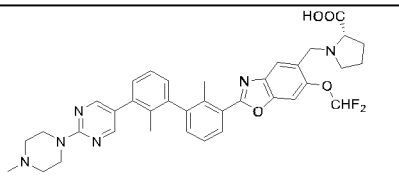
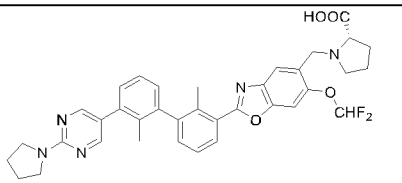
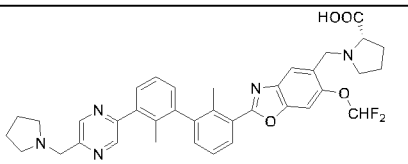
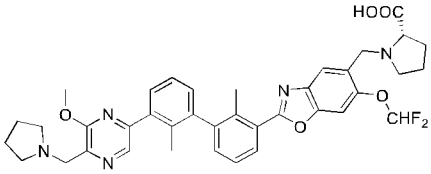
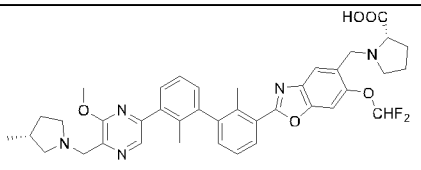
217	((6-(difluoromethoxy)-2-(4"-(((2-hydroxyethyl)amino)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		642.3
218	((6-(difluoromethoxy)-2-(2,2',3"-trimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline		666.3
219	((2-(3"-chloro-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline		686.3
220	((6-(difluoromethoxy)-2-(2"-fluoro-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline		670.3
221	((2-(2'-bromo-2"-fluoro-2-methyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline		733.2
222	((2-(2'-chloro-2"-fluoro-2-methyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline		690.2
223	((2-(2'-chloro-2"-fluoro-2-methyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		690.2
224	((2-(2'-chloro-2"-fluoro-2-methyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline		690.2
225	((6-(difluoromethoxy)-2-(4"-guanidino-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		626.3
226	((6-(difluoromethoxy)-2-(4"-(((3-(dimethylamino)propyl)(methyl)amino)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		697.4
227	((6-(difluoromethoxy)-2-(4"-((3-methoxypyrrolidin-1-yl)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		682.3

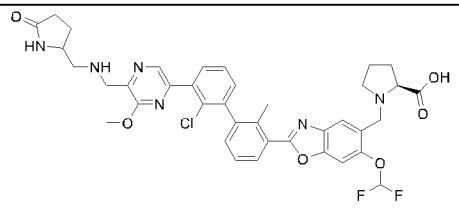
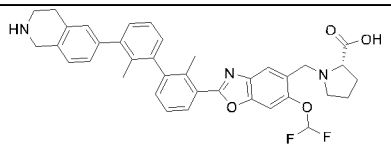
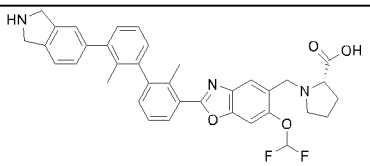
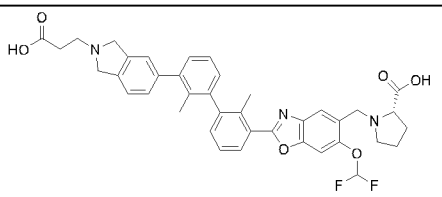
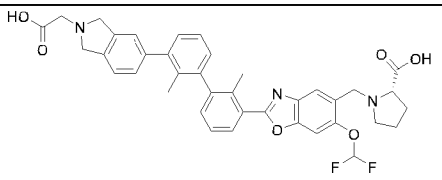
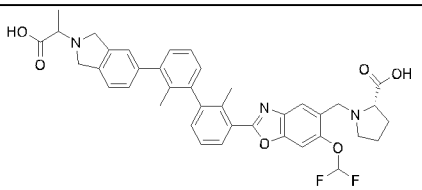
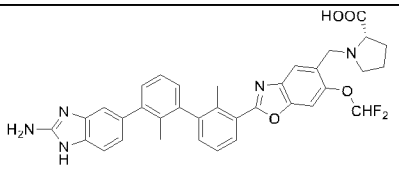
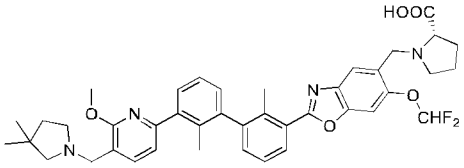
228	((6-(difluoromethoxy)-2-(4"-((3-(dimethylamino)pyrrolidin-1-yl)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		695.3
229	((2-(3"-chloro-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		686.3
230	((6-(difluoromethoxy)-2-(2,2',3"-trimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		666.3
231	((2-(2"-chloro-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		686.3
232	((6-(difluoromethoxy)-2-(2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-3"-(trifluoromethoxy)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		736.3
233	((6-(difluoromethoxy)-2-(2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-3"-(trifluoromethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		720.3
234	((6-(difluoromethoxy)-2-(2,2',3",5"-tetramethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		680.3
235	((6-(difluoromethoxy)-2-(3"-fluoro-5"-methoxy-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		700.3
236	((2-(3"-carboxy-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		696.3
237	((6-(difluoromethoxy)-2-(4"-((3,3-dimethylazetidin-1-yl)methyl)-3"-fluoro-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		684.3
238	((6-(difluoromethoxy)-2-(3"-fluoro-2,2'-dimethyl-4"-((3-methylpyrrolidin-1-yl)methyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		684.3

239	((6-(difluoromethoxy)-2-(3"-fluoro-4"-(((2-hydroxyethyl)amino)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		660.3
240	((2-(3"-cyano-4"-(((S)-3-(hydroxymethyl)pyrrolidin-1-yl)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		707.3
241	((6-(difluoromethoxy)-2-(3"-fluoro-4"-(isoindolin-2-ylmethyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline		718.3
248	((6-(difluoromethoxy)-2-(3"-fluoro-2,2'-dimethyl-4"-(((S)-3-phenylpyrrolidin-1-yl)methyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline		746.3
249	((6-(difluoromethoxy)-2-(3"-(4-fluorophenethoxy)-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline		790.3
250	((2-(3"-(cyclopropylmethoxy)-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline		722.3
251	((2-(4"-(((R)-3-(1H-tetrazol-5-yl)pyrrolidin-1-yl)methyl)-3"-fluoro-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline		738.3
252	((2-(4"-(((S)-3-((benzyloxy)methyl)pyrrolidin-1-yl)methyl)-3"-fluoro-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline		790.3
253	((6-(difluoromethoxy)-2-(2"-fluoro-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		670.3
254	((6-(difluoromethoxy)-2-(3",5"-dimethoxy-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline hydrochloride		748.3
255	((6-(difluoromethoxy)-2-(2,2'-dimethyl-4"-(pyrrolidin-2-yl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		638.3

256	((2-(4"-((S)-amino(carboxy)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		642.2
257	((6-(difluoromethoxy)-2-(4"-(((S)-3-((S)-2-((methoxycarbonyl)amino)-3-methylbutanamido)pyrrolidin-1-yl)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		824.4
258	((6-(difluoromethoxy)-2-(3"-fluoro-2,2'-dimethyl-4"-((5-ureidoisoindolin-2-yl)methyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		776.3
260	((6-(difluoromethoxy)-2-(3"-fluoro-2,2'-dimethyl-4"-((3-ureidopyrrolidin-1-yl)methyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		728.3
262	((6-(difluoromethoxy)-2-(3'-(4-fluoro-6-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		671.3
263	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(6-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		653.3
264	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		653.3
265	((6-(difluoromethoxy)-2-(3'-(5-fluoro-6-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		671.3
266	((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(pyrrolidin-1-ylmethyl)pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		683.3
267	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(6-oxo-5-(pyrrolidin-1-ylmethyl)-1,6-dihydropyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		669.3

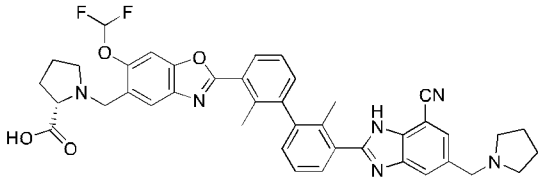
268	((6-(difluoromethoxy)-2-(2'-(difluoromethyl)-3'-(5-fluoro-6-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-2-methyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		707.3
269	((6-(difluoromethoxy)-2-(3'-(5-fluoro-6-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-2'-(fluoromethyl)-2-methyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		689.3
270	((6-(difluoromethoxy)-2-(3'-(2-fluoro-6-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		671.3
271	((6-(difluoromethoxy)-2-(3'-(5-((3,3-dimethylazetidin-1-yl)methyl)-6-methoxypyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		697.3
272	((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(((R)-3-methylpyrrolidin-1-yl)methyl)pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		697.3
273	((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(((S)-3-methylpyrrolidin-1-yl)methyl)pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-D-proline		697.3
274	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)-4-vinylpyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		679.3
275	((6-(difluoromethoxy)-2-(3'-(5-((3-(difluoromethyl)pyrrolidin-1-yl)methyl)-6-methoxypyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		733.3
276	((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-((((5-oxopyrrolidin-2-yl)methyl)amino)methyl)pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		726.3
277	((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(((S)-2-methylpyrrolidin-1-yl)methyl)pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		697.3

278	((2-(3'-(5-(((1s,4s)-7-azabicyclo[2.2.1]heptan-7-yl)methyl)-6-methoxypyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		709.3
279	((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(((R)-2-methylpyrrolidin-1-yl)methyl)pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		697.3
280	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)thiophen-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		658.3
281	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(2-(pyrrolidin-1-ylmethyl)pyrimidin-5-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		654.3
282	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(2-(4-methylpiperazin-1-yl)pyrimidin-5-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		669.3
283	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(2-(pyrrolidin-1-yl)pyrimidin-5-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		640.3
284	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)pyrazin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		654.3
285	((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(pyrrolidin-1-ylmethyl)pyrazin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		684.3
286	((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(((R)-3-methylpyrrolidin-1-yl)methyl)pyrazin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		698.3

287	((2-(2'-chloro-3'-(6-methoxy-5-((((5-oxopyrrolidin-2-yl)methyl)amino)methyl)pyrazin-2-yl)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		747.2
288	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(1,2,3,4-tetrahydroisoquinolin-6-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		624.3
289	((6-(difluoromethoxy)-2-(3'-(isoindolin-5-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		610.2
290	((2-(3'-(2-(2-carboxyethyl)isoindolin-5-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		682.3
291	((2-(3'-(2-(carboxymethyl)isoindolin-5-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		668.3
292	((2-(3'-(2-(1-carboxyethyl)isoindolin-5-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		682.3
293	((2-(3'-(2-amino-1H-benzo[d]imidazol-5-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		624.2
294	((6-(difluoromethoxy)-2-(3'-(5-((3,3-dimethylpyrrolidin-1-yl)methyl)-6-methoxypyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		711.3

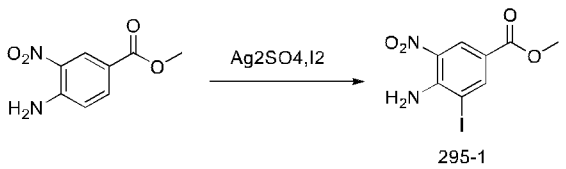
Example 295 Synthesis of compound 295

((2-(3'-(7-cyano-5-(pyrrolidin-1-ylmethyl)-1H-benzo[d]imidazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline



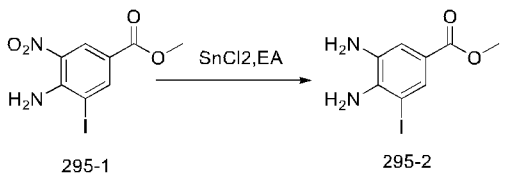
Compound 295

Step 1: Preparation of methyl 4-amino-3-iodo-5-nitrobenzoate



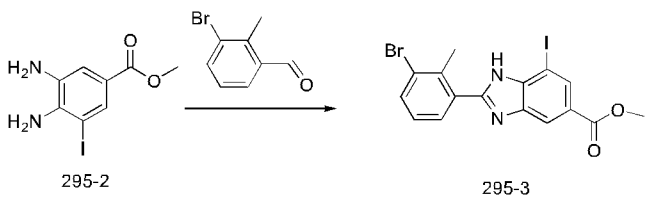
Methyl 4-amino-3-nitro-benzoate (5 g) was added to a mixture of Ag_2SO_4 (7.93 g) and I2 (6.47 g) in EtOH (20 mL) at room temperature. The mixture was stirred at room temperature overnight. The reaction mixture was diluted with water (20 mL) and extracted with ethyl acetate. The organic layers were washed with aqueous $Na_2S_2O_3$, dried over $MgSO_4$ and evaporated to dryness. The residue was purified by chromatography on silica gel to give the desired product methyl 4-amino-3-iodo-5-nitro-benzoate (7 g) as a yellow solid.

Step 2: Preparation of methyl 3,4-diamino-5-iodobenzoate



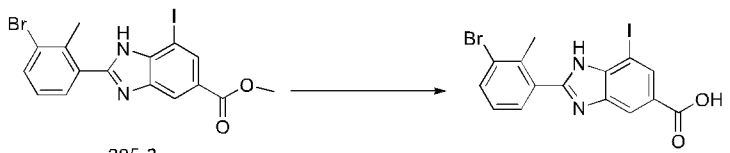
To a solution of compound 295-1 (3 g) in EA (30 mL) was added $SnCl_2$ (8.42 g). The reaction mixture was stirred at 70°C for 16 hrs. EA (50 mL) was added to the reaction mixture and the organic layer was washed with aqueous $NaHCO_3$, dried over $MgSO_4$ and evaporated to dryness. The residue was purified by chromatography on silica gel to give the desired product methyl 3,4-diamino-5-iodo-benzoate (2.6 g) as a yellow solid.

Step 3: Preparation *of methyl 2-(3-bromo-2-methylphenyl)-7-iodo-1H-benzo[d]imidazole-5-carboxylate*



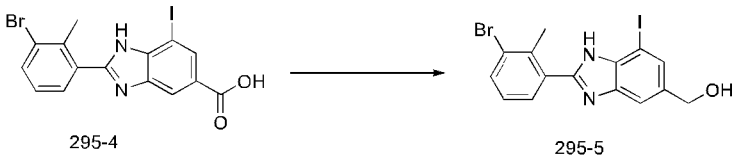
A mixture of compound 295-2 (2.6 g), 3-bromo-2-methyl-benzaldehyde (1.77 g) and AcOH (30 mL) was stirred at 80°C for 16 hrs. EA (50 mL) was added to the reaction mixture and the organic layer was washed with water, dried over $MgSO_4$ and evaporated to dryness. The residue was purified by chromatography on silica gel to give the desired product methyl 2-(3-bromo-2-methyl-phenyl)-7-iodo-1H-benzimidazole-5-carboxylate (3.2 g) as a yellow solid.

Step 4: Preparation of 2-(3-bromo-2-methylphenyl)-7-iodo-1H-benzo[d]imidazole-5-carboxylic acid



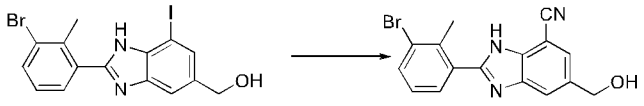
To a solution of compound 295-3 (2 g) in MeOH (20 mL) was added the solution of NaOH (849.10 mg) in H_2O (6 mL). The reaction mixture was stirred at 50°C overnight. The mixture was concentrated. H_2O (10 mL) was added to the mixture and adjusted pH to 5 with 2N HCl, The precipitate was filtered and the filter cake was washed with H_2O. The product was dried in a vacuum oven (45°C, 3hours) to yield 2-(3-bromo-2-methyl-phenyl)-7-iodo-1H-benzimidazole-5-carboxylic acid (1.8 g) of the title compound as an off-white solid.

Step 5: Preparation of (2-(3-bromo-2-methylphenyl)-7-iodo-1H-benzo[d]imidazol-5-yl)methanol



Borane-tetrahydrofuran complex (20mL) was added to a solution of compound 295-4 (1.8 g) in THF(20mL) at -30°C. The reaction mixture was then stirred at 60°C for 16 hrs. The mixture was cooled to room temperature and 2N HCl (20mL) was added. After 10 mins, the mixture was diluted withethyl acetate and washed with water. The organic layer was dried over $MgSO_4$ and evaporated to dryness. The residue was purified by chromatography on silica gel to give the desired product [2-(3-bromo-2-methyl-phenyl)-7-iodo-1H-benzimidazol-5-yl] methanol (1 g) as a white solid.

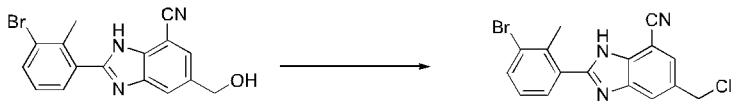
Step 6: Preparation of 2-(3-bromo-2-methylphenyl)-5-(hydroxymethyl)-1H-benzo[d]imidazole-7-carbonitrile



295-5 295-6

A mixture of compound 295-5 (500 mg), $Zn(CN)_2$ (66.02 mg) $Pd(PPh_3)_4$ (130.34 mg) in DMF (10 mL) was stirred at 90°C for 3 hrs under nitrogen. The reaction mixture was diluted with water (10 mL) and extracted with ethyl acetate. Then, the organic layer was washed with aqueous NaCl, dried over $MgSO_4$ and evaporated to dryness. The residue was purified by chromatography on silica gel to give the desired product 2-(3-bromo-2-methyl-phenyl)-6-(hydroxymethyl)-3H-benzimidazole-4-carbonitrile (150 mg) as a yellow oil.

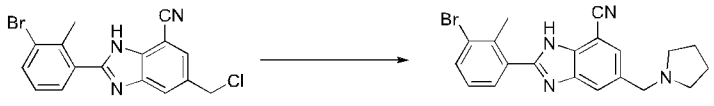
Step 7: Preparation of 2-(3-bromo-2-methylphenyl)-5-(chloromethyl)-1H-benzo[d]imidazole-7-carbonitrile



295-6 295-7

This compound was prepared using similar procedures as described as step 2 in example 1, with compound 295-6 replacing compound 1-1. The mixture was concentrated to give the title compound.

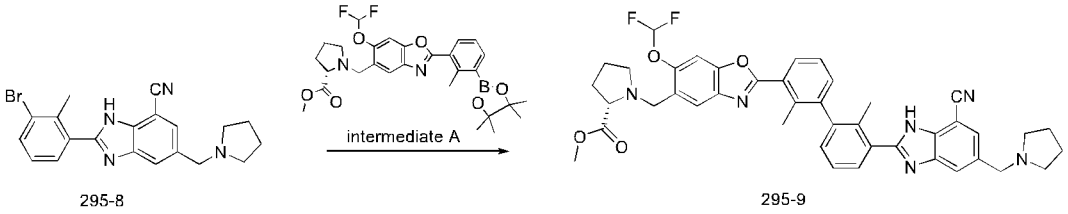
Step 8: Preparation of 2-(3-bromo-2-methylphenyl)-5-(pyrrolidin-1-ylmethyl)-1H-benzo[d]imidazole-7-carbonitrile



295-7 295-8

This compound was prepared using similar procedures as described as step 3 in example 1, with compound 295-7 replacing compound 1-2, and with pyrrolidine replacing (1S, 2R)-2-aminocyclopentan-1-ol. The crude product was purified by chromatography on silica gel to give the title compound.

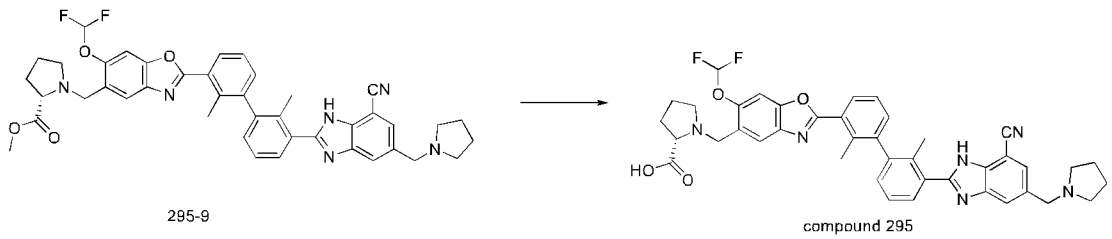
Step 9: Preparation of methyl ((2-(3'-(7-cyano-5-(pyrrolidin-1-ylmethyl)-1H-benzo[d]imidazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-prolinate



295-8 295-9

This compound was prepared using similar procedures as described as step 1 in example 1, with compound 295-8 replacing compound a-6. The crude product was purified by chromatography on silica gel to give the title compound.

Step 10: Preparation of ((2-(3'-(7-cyano-5-(pyrrolidin-1-ylmethyl)-1H-benzo[d]imidazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline

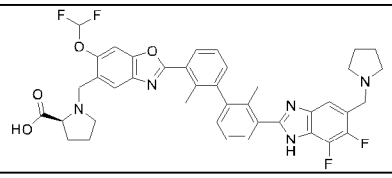
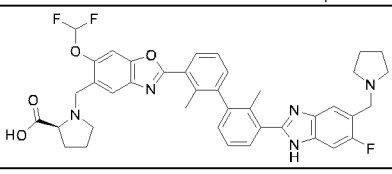


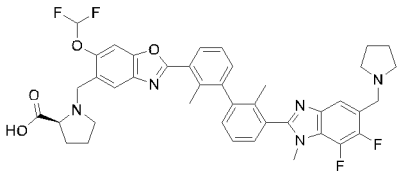
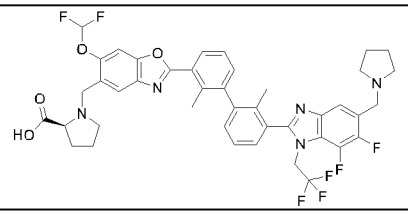
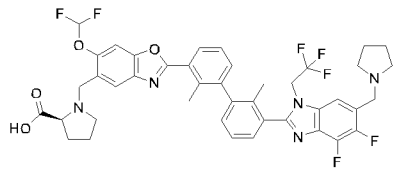
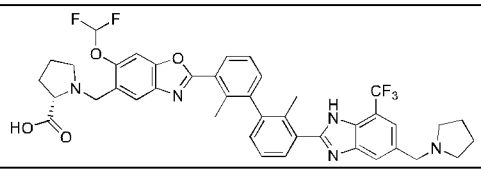
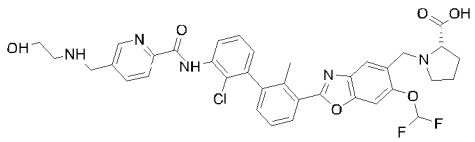
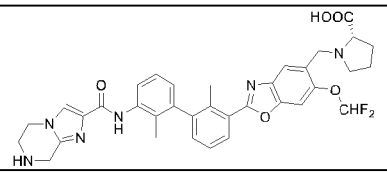
295-9 compound 295

This compound was prepared using similar procedures as described as step 5 in example 1, with compound 295-9 replacing compound 1-4.The crude product was purified by pre-HPLC to give the desired product (2S)-1-[[2-[3-[3-[7-cyano-5-(pyrrolidin-1-ylmethyl)-1H-benzimidazol-2-yl]-2-methyl-phenyl]-2-methyl-phenyl]-6-(difluoromethoxy)-1,3-benzoxazol-5-yl]methyl]pyrrolidine-2-carboxylic acid. LC-MS(m/z):717.3$(M+H)^+$.

The compounds of table 7 were prepared in a similar manner to Example 295 via different reaction starting materials and suitable reagents.

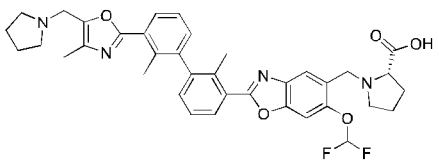
Table 7

EX No.	Chemical Name	Structure	Physical Data (MS) $(M+H)^+$
296	((2-(3'-(6,7-difluoro-5-(pyrrolidin-1-ylmethyl)-1H-benzo[d]imidazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		728.3
297	((6-(difluoromethoxy)-2-(3'-(6-fluoro-5-(pyrrolidin-1-ylmethyl)-1H-benzo[d]imidazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		710.3

298	((2-(3'-(6,7-difluoro-1-methyl-5-(pyrrolidin-1-ylmethyl)-1H-benzo[d]imidazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		742.3
299	((2-(3'-(6,7-difluoro-5-(pyrrolidin-1-ylmethyl)-1-(2,2,2-trifluoroethyl)-1H-benzo[d]imidazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		810.3
300	((2-(3'-(4,5-difluoro-6-(pyrrolidin-1-ylmethyl)-1-(2,2,2-trifluoroethyl)-1H-benzo[d]imidazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		810.3
301	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)-7-(trifluoromethyl)-1H-benzo[d]imidazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		760.3
302	((2-(2'-chloro-3'-(5-(((2-hydroxyethyl)amino)methyl)picolinamido)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline		706.2
303	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine-2-carboxamido)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		657.3

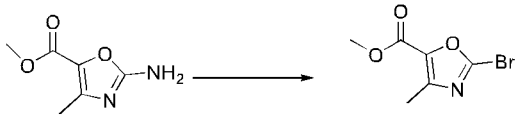
Example 304 Synthesis of compound 304

((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(4-methyl-5-(pyrrolidin-1-ylmethyl)oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline



Compound 304

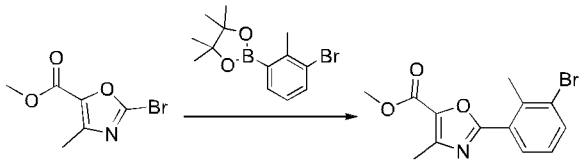
Step-1: methyl 2-bromo-4-methyl-oxazole-5-carboxylate



304-1

tert-Butyl nitrite (2.24 g) was added to a suspension of methyl 2-amino-4-methyl-oxazole-5-carboxylate (1.7 g) $CuBr_2$ (7.28 g) in acetonitrile(20mL). The mixture was stirred at room temperature overnight. The reaction mixture was diluted with water (50 mL) and extracted with ethyl acetate. Then, the organic layer was washed with aqueous NaCl, dried over $MgSO_4$ and evaporated to dryness. The residue was purified by chromatography on silica gel to give the desired product methyl 2-bromo-4-methyl-oxazole-5-carboxylate (800 mg) as a white solid.

Step-2: Preparation of methyl 2-(3-bromo-2-methyl-phenyl)-4-methyl-oxazole-5-carboxylate



304-1 304-2

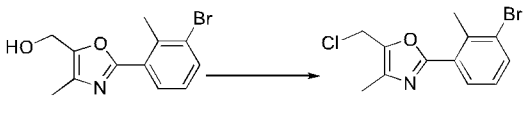
This compound was prepared using similar procedures as described as step 1 in example 1. The crude product was purified by chromatography on silica gel to give the title compound.

Step-3: Preparation of [2-(3-bromo-2-methyl-phenyl)-4-methyl-oxazol-5-yl]methanol

304-2 304-3

This compound was prepared using similar procedures as described as step 5 in example A, with compound 304-2 replacing compound a-4. The crude product was purified by chromatography on silica gel to get the title compound.

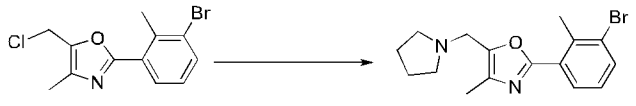
Step-4: Preparation of 2-(3-bromo-2-methyl-phenyl)-5-(chloromethyl)-4-methyl-oxazole



304-3 304-4

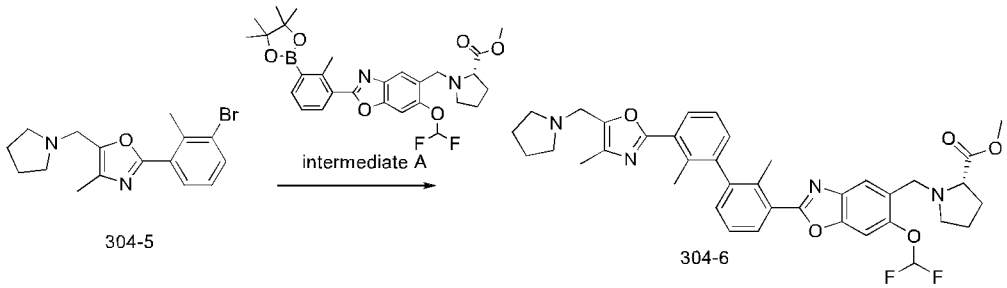
This compound was prepared using similar procedures as described as step 2 in example 1, with compound 304-3 replacing compound 1-1. The mixture was concentrated to give the title compound.

Step-5: Preparation of 2-(3-bromo-2-methyl-phenyl)-4-methyl-5-(pyrrolidin-1-ylmethyl)oxazole



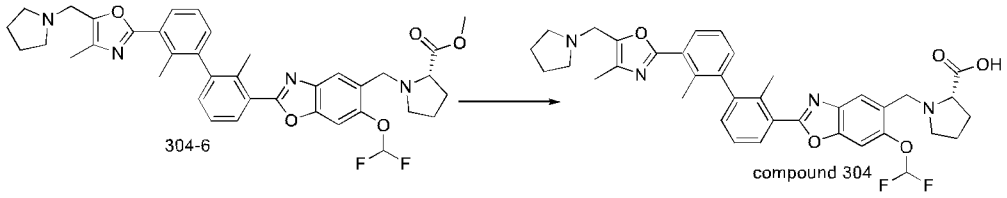
This compound was prepared using similar procedures as described as step 3 in example 1 ,with compound 304-4 replacing compound 1-2, and with pyrrolidine replacing (1S, 2R)-2-aminocyclopentan-1-ol. The crude product was purified by chromatography on silica gel to get the title compound.

Step-6: Preparation of methyl (2S)-1-[[6-(difluoromethoxy)-2-[2-methyl-3-[2-methyl-3-[4-methyl-5-(pyrrolidin-1-ylmethyl)oxazol-2-yl]phenyl]phenyl]-1,3-benzoxazol-5-yl]methyl]pyrrolidine-2-carboxylate



This compound was prepared using similar procedures as described as step 1 in example 1, with compound 304-5 replacing compound a-6. The crude product was purified by chromatography on silica gel to get the title compound.

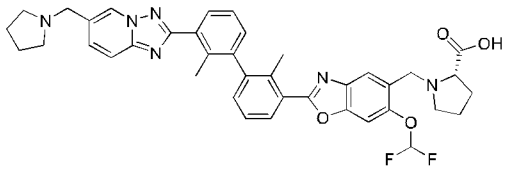
Step-7: Preparation of ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(4-methyl-5-(pyrrolidin-1-ylmethyl)oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline



This compound was prepared using similar procedures as described as step 5 in example 1, with compound 304-6 replacing compound 1-4. The crude product was purified by pre-HPLC to give the title compound. LC-MS(m/z):657.3$(M+H)^+$.

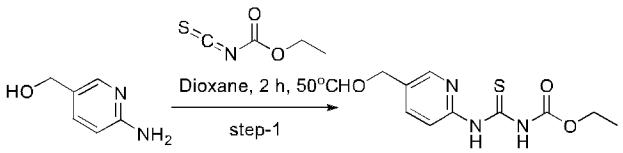
Example 305 Synthesis of compound 305

((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(6-(pyrrolidin-1-ylmethyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline



Compound 305

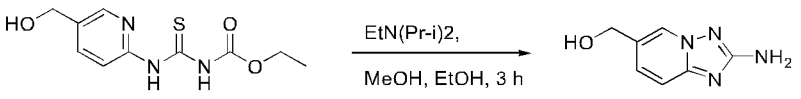
Step-1: Preparation of ethyl N-[[5-(hydroxymethyl)-2-pyridyl]carbamothioyl]carbamate



305-1

To a solution of (6-aminopyridin-3-yl)methanol (5g) in 1,4-dioxane (25mL) was added ethyl N-(thioxomethylene)carbamate (7.92 g). The reaction mixture was stirred at 50°C for 3 hrs. The mixture was concentrated to get a residue. The residue was directly used for the next step.

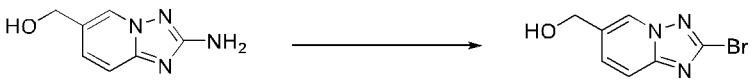
Step-2: Preparation of (2-amino-[1,2,4]triazolo[1,5-a]pyridin-6-yl)methanol



305-1 305-2

Hydroxylamine hydrochloride (5.13g) was added to a solution of compound 305-1 (9.5 g) in methanol (15 mL)/ethanol (15 mL), followed by N, N-diisopropylethylamine (9.62g). The reaction mixture was then stirred at 50°C for 3 hrs. The crude was cooled and the precipitate was filtered to give the desired product (5.0g) as green oil.

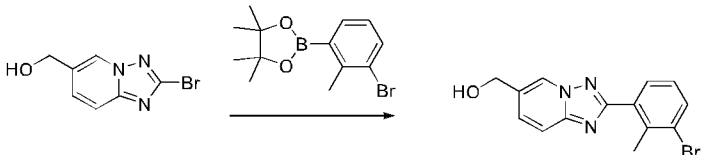
Step-3: Preparation of (2-bromo-[1,2,4]triazolo[1,5-a]pyridin-6-yl)methanol



305-2 305-3

tert-Butyl nitrite (5.6 g) was added to a suspension of compound 305-2 (5 g) and copper(II) bromide (1.22 g) in acetonitrile (50mL). The mixture was stirred at room temperature for 1 h. The reaction mixture was diluted with DCM and washed with water. The organic phase was dried, filtered and concentrated to almost dry. The residue was purified by chromatography on silica gel to give the desired product (3.2 g) as a white solid.

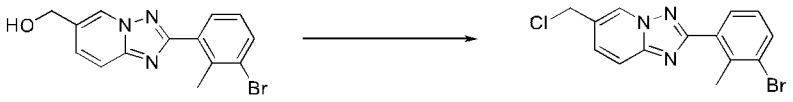
Step-4: Preparation of [2-(3-bromo-2-methyl-phenyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl]methanol



305-3 305-4

This compound was prepared using similar procedures as described as step 1 in example 1. The residue was purified by chromatography on silica gel to give the title compound.

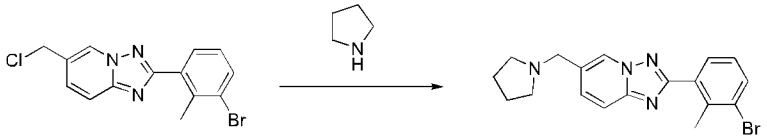
Step-5: Preparation of 2-(3-bromo-2-methyl-phenyl)-6-(chloromethyl)-[1,2,4]triazolo[1,5-a]pyridine



305-4 305-5

This compound was prepared using similar procedures as described as step 2 in example 1, with compound 305-4 replacing compound 1-1. The crude product was used directly in the next step.

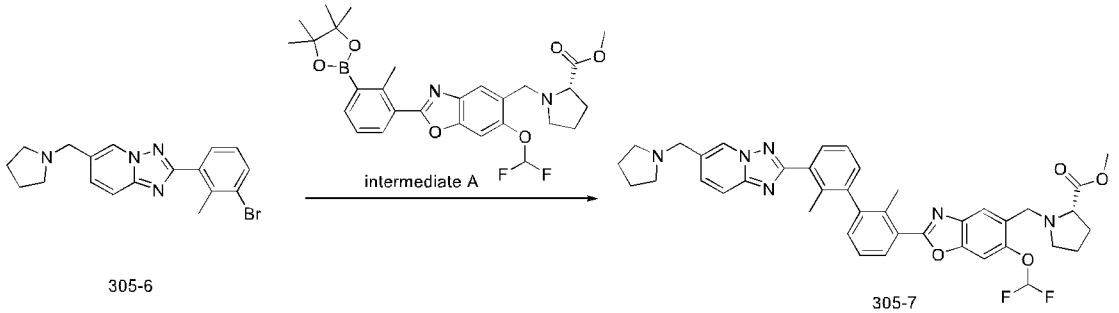
Step-6: Preparation of 2-(3-bromo-2-methyl-phenyl)-6-(pyrrolidin-1-ylmethyl)-[1,2,4]triazolo[1,5-a]pyridine



305-5 305-6

This compound was prepared using similar procedures as described as step 3 in example 1, with compound 305-5 replacing compound 1-2, and with pyrrolidine replacing (1S, 2R)-2-aminocyclopentan-1-ol. The crude product was purified by chromatography on silica gel to get the title compound.

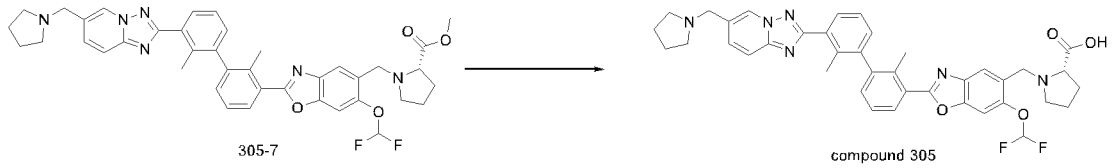
Step-7: Preparation of methyl (2S)-1-[[6-(difluoromethoxy)-2-[2-methyl-3-[2-methyl-3-[6-(pyrrolidin-1-ylmethyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl]phenyl]phenyl]-1,3-benzoxazol-5-yl]methyl]pyrrolidine-2-carboxylate



305-6 305-7

This compound was prepared using similar procedures as described as step 1 in example 1, with compound 305-6 replacing compound a-6. The crude product was purified by chromatography on silica gel to get the title compound.

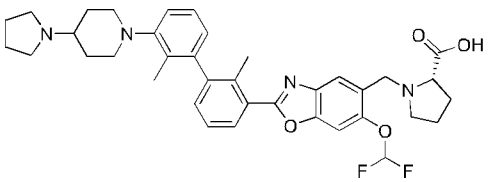
Step-8: Preparation of ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(6-(pyrrolidin-1-ylmethyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline



This compound was prepared using similar procedures as described as step 5 in example 1, with compound 305-7 replacing compound 1-4. The crude product was purified by pre-HPLC to give the title compound. LC-MS(m/z):693.3$(M+H)^+$.

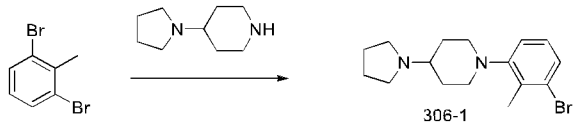
Example 306 Synthesis of compound 306

((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(4-(pyrrolidin-1-yl)piperidin-1-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline



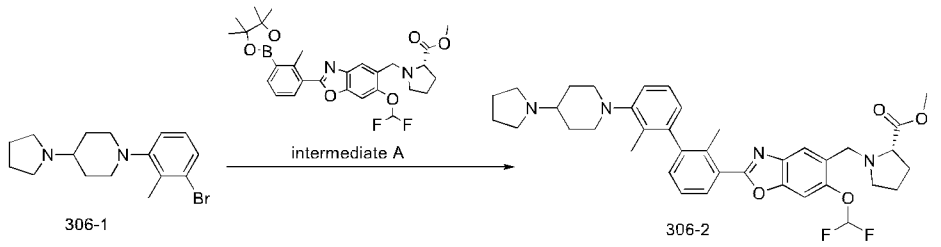
Compound 306

Step-1: Preparation of 1-(3-bromo-2-methyl-phenyl)-4-pyrrolidin-1-yl-piperidine



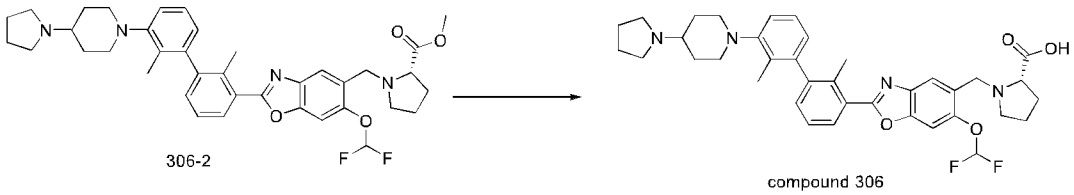
A mixture of 1,3-dibromo-2-methyl-benzene (1 g), 4-pyrrolidin-1-ylpiperidine (617.18 mg), Cs_2CO_3 (3.91 g), $Pd_2(dba)_3$ (366.10 mg), and xantphos (462.53 mg) in toluene (20 mL) was stirred at 100°C overnight under nitrogen. The mixture was concentrated to get a residue. The residue was purified by chromatography on silica gel to give the desired product 1-(3-bromo-2-methyl-phenyl)-4-pyrrolidin-1-yl-piperidine (450 mg) as a red oil.

Step-2: Preparation of methyl (2S)-1-[[6-(difluoromethoxy)-2-[2-methyl-3-[2-methyl-3-(4-pyrrolidin-1-yl-1-piperidyl)phenyl]phenyl]-1,3-benzoxazol-5-yl]methyl]pyrrolidine-2-carboxylate



This compound was prepared using a similar procedure as described as step1 in example 1, with compound 306-1 replacing compound a-6. The crude product was purified by chromatography on silica gel to get the title compound.

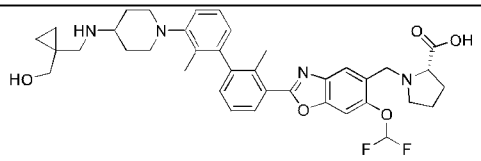
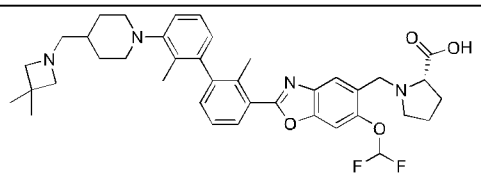
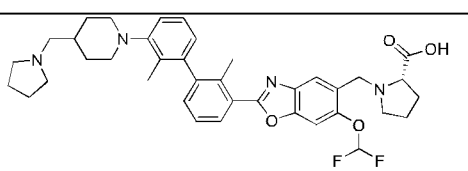
Step-3: Preparation of ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(4-(pyrrolidin-1-yl)piperidin-1-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline



This compound was prepared using a similar procedure as described as step5 in example 1, with compound 306-2 replacing compound 1-4. The crude product was purified by pre-HPLC to give the title compound. LC-MS (m/z):645.3$(M+H)^+$.

The compounds of table 8 were prepared in a similar manner to Examples 304-306 via different reaction starting materials and suitable reagents.

Table 8

EX No.	Chemical Name	Structure	Physical Data (MS) $(M+H)^+$
307	((6-(difluoromethoxy)-2-(3'-(4-(((1-(hydroxymethyl)cyclopropyl)methyl)amino)piperidin-1-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		675.3
308	((6-(difluoromethoxy)-2-(3'-(4-((3,3-dimethylazetidin-1-yl)methyl)piperidin-1-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		673.4
309	((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(4-(pyrrolidin-1-ylmethyl)piperidin-1-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline		659.3

The ^{1}HNMR data of compounds 34, 61, 85, 88, 93, 113, 127, 130, 131, 135, 142 and 146 are as follws:

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.24 (s, 1H), 8.17 (dd, J = 8.0, 2.2 Hz, 2H), 8.08 (s, 1H), 7.88 (s, 1H), 7.81 (s, 1H), 7.64 – 7.51 (m, 2H), 7.49 – 7.20 (m, 4H), 4.52 (s, 2H), 4.38 – 4.12 (m, 2H), 3.94 – 3.84 (m, 4H), 3.26 – 2.86 (m, 3H), 2.45 (s, 6H), 2.37 – 1.71 (m, 4H), 1.31 (d, J = 43.4 Hz, 6H). (Compound 34)

^{1}H NMR (500 MHz, Chloroform-d) δ 8.30 – 8.03 (m, 4H), 7.66 – 7.54 (m, 2H), 7.49 – 7.41 (m, 2H), 7.40 – 7.35 (m, 2H), 7.10 – 6.77 (m, 2H), 4.86 – 4.18 (m, 5H), 3.94 – 3.57 (m, 3H), 3.43 – 3.25 (m, 2H), 2.71 – 2.55 (m, 2H), 2.48 (d, J = 3.7 Hz, 6H), 2.37 – 1.58 (m, 6H), 1.27 – 1.08 (m, 3H).(Compound 61)

^{1}H NMR (500 MHz, Chloroform-d) δ 8.13 (dd, J = 7.8, 6.1 Hz, 2H), 7.99 (d, J = 9.8 Hz, 2H), 7.52 (d, J = 17.9 Hz, 2H), 7.48 – 7.42 (m, 2H), 7.37 – 7.34 (m, 2H), 6.83 (t, J = 71.9 Hz, 1H), 6.80 (t, J = 71.9Hz, 1H), 4.29 (d, J = 25.2 Hz, 4H), 3.70 (s, 4H), 3.42 (dd, J = 10.6, 4.4 Hz, 1H), 3.21 (q, J = 8.3 Hz, 2H), 3.09 (d, J = 22.7 Hz, 2H), 2.46 (d, J = 7.9 Hz, 6H), 2.34 – 2.22 (m, 2H), 1.35 (s, 6H). (Compound 85)

^{1}H NMR (500 MHz, Chloroform-d) δ 8.36 (s, 1H), 8.22 (dd, J = 7.9, 1.5 Hz, 1H), 8.17 – 8.07 (m, 2H), 7.99 (s, 1H), 7.59 (s, 1H), 7.46 (dt, J = 12.7, 7.7 Hz, 2H), 7.42 – 7.34 (m, 2H), 6.93 (t, J = 72.1 Hz, 1H), 4.78 – 4.62 (m, 2H), 4.52 (t, J = 12.8 Hz, 2H), 4.21 (t, J = 8.0 Hz, 1H), 3.87 – 3.58 (m, 3H), 3.21-3.00 (m, 2H), 2.75 – 2.53 (m, 3H), 2.47 (d, J = 15.4 Hz, 6H), 2.39-2.23 (m, 2H), 2.16 (t, J = 7.9 Hz, 2H), 1.78 (d, J = 62.1 Hz, 1H), 1.21 – 1.10 (m, 3H). (Compound 88)

^{1}H NMR (500 MHz, Chloroform-d) δ 8.18 (d, J = 7.9 Hz, 1H), 8.06 (d, J = 7.9 Hz, 1H), 7.93 – 7.76 (m, 2H), 7.55 (s, 1H), 7.49 – 7.26 (m, 5H), 6.76 (t, J = 72.9 Hz, 1H), 4.29 – 3.39 (m, 6H), 3.23 – 2.91 (m, 6H), 2.38-2.47(d, J = 25.5Hz, 6H), 2.09 – 1.60 (m, 3H),1.23 (s, 6H). (Compound 93)

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.38 (s, 1H), 8.26 (s, 1H), 8.20 (dd, J = 7.9, 1.4 Hz, 1H), 8.13 (ddd, J = 23.5, 7.9, 1.5 Hz, 1H), 7.96 (d, J = 10.1 Hz, 1H), 7.72 (d, J = 13.9 Hz, 1H), 7.61 – 7.49 (m, 2H), 7.45 (ddd, J = 13.6, 7.6, 1.5 Hz, 2H), 7.38 (d, J = 71.9 Hz, 1H), 3.96 (s, 2H), 3.44-3.22 (m, 5H), 3.11-2.99 (m, 2H), 2.57 (q, J = 8.5 Hz, 1H), 2.45 (d, J = 5.8 Hz, 6H), 2.19-2.06 (m, 1H), 1.93 – 1.64 (m, 4H), 1.22 (d, J = 7.5 Hz, 6H). (Compound 113)

^{1}H NMR (500 MHz, Chloroform-d) δ 8.24 (dd, J = 7.9, 1.4 Hz, 1H), 8.17 – 8.07 (m, 2H), 8.03 (s, 1H), 7.79 (s, 1H), 7.60 (s, 1H), 7.48 (dt, J = 15.0, 7.7 Hz, 2H), 7.43 – 7.35 (m, 2H), 6.94 (t, J = 71.9 Hz, 1H), 4.60 (d, J = 13.1 Hz, 1H), 4.50 (d, J = 13.2 Hz, 1H), 3.97 (s, 3H), 3.71 –

3.60 (m, 1H), 3.15 (q, J = 9.9 Hz, 1H), 2.76 (s, 4H), 2.47(s, 6H), 2.33-2.24 (m, 1H), 2.15-2.06 (m, 1H), 2.06 – 1.97 (m, 2H), 1.91 (q, J = 3.5, 3.0 Hz, 4H). (Compound 127)

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.20 (dd, J = 7.9, 1.4 Hz, 1H), 8.16 (dd, J = 7.9, 1.4 Hz, 1H), 8.11 (d, J = 1.5 Hz, 1H), 7.97 (s, 1H), 7.88 (d, J = 1.5 Hz, 1H), 7.73 (s, 1H),7.63 – 7.51 (m, 2H), 7.48 (dd, J = 7.6, 1.4 Hz, 1H), 7.44 (dd, J = 7.6, 1.4 Hz, 1H), 7.38 (t, J = 73.7 Hz, 1H), 3.96 (s, 2H), 3.79 – 3.68 (m, 2H), 3.38– 3.31 (m, 1H), 3.09– 3.03 (m, 1H), 2.74– 2.48 (m, 5H), 2.44 (d, J = 2.9 Hz, 6H), 2.26 – 1.68 (m, 6H), 1.36– 1.20 (m, 1H), 0.99 (d, J = 6.7 Hz, 3H). (Compound 130)

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.21 (dd, J = 7.9, 1.4 Hz, 1H), 8.19 (s, 1H), 8.15 (dd, J = 7.9, 1.4 Hz, 1H), 7.97 (s, 1H), 7.95 (s, 1H), 7.73 (s, 1H), 7.63 – 7.51 (m, 2H), 7.48 (dd, J = 7.6, 1.4 Hz, 1H), 7.44 (dd, J = 7.5, 1.4 Hz, 1H), 7.38 (t, J = 73.7 Hz, 1H), 3.97 (s, 2H), 3.92 – 3.86 (m, 2H), 3.38 – 3.31 (m, 1H), 3.11 – 3.05 (m, 1H), 2.83 – 2.51 (m, 5H), 2.44 (d, J = 4.1 Hz, 6H), 2.31 – 1.70(m, 6H), 1.46 – 1.14 (m, 1H), 1.00 (d, J = 6.3 Hz, 3H). (Compound 131)

^{1}H NMR (500 MHz, Chloroform-d) δ 8.25 (d, J = 7.8 Hz, 1H), 8.14 (dd, J = 7.9, 1.3 Hz, 1H), 8.10 (s, 1H), 7.94 (s, 1H), 7.77 (s, 1H), 7.61 (s, 1H), 7.48 (dt, J = 15.2, 7.7 Hz, 2H), 7.42 – 7.34 (m, 2H), 6.93 (t, J = 71.9 Hz, 1H), 4.55 (d, J = 13.0 Hz, 1H), 4.37 (d, J = 13.1 Hz, 2H), 3.94 – 3.35 (m, 5H), 3.17 – 2.82 (m, 4H), 2.51 (s, 3H), 2.47 (s, 3H), 2.47 – 2.29 (m, 2H), 2.16 – 1.46 (m, 10H). (Compound 135)

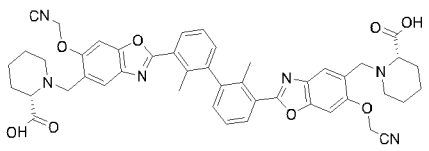
^{1}H NMR (500 MHz, DMSO-d_6) δ 8.35 – 8.30 (m, 1H), 8.23 (dd, J = 8.0, 1.5 Hz, 1H), 8.18 (dt, J = 7.9, 1.3 Hz, 1H), 8.12 (d, J = 1.4 Hz, 1H), 8.08 (s, 1H), 7.89 (s, 1H), 7.61 (dt, J = 13.6, 7.7 Hz, 2H), 7.57 – 7.45 (m, 2H), 7.40 (t, J = 73.2 Hz, 1H), 4.62 – 4.25 (m, 4H), 3.58 – 3.07 (m, 5H),2.52 – 2.50 (m, 1H), 2.49 – 2.48 (m, 4H), 2.45 (d, J = 5.5 Hz, 6H), 2.26 – 1.80 (m, 4H). (Compound 142)

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.35 (s, 1H), 8.23 (d, J = 7.9 Hz, 1H), 8.18 (d, J = 7.8 Hz, 1H), 8.13 – 8.07 (m, 2H), 7.87 (s, 1H), 7.70 (s, 1H), 7.60 (dt, J = 14.9, 7.7 Hz, 2H), 7.56 – 7.44 (m, 2H), 7.32 (t, J = 73.2 Hz, 1H),4.56 – 4.01 (m, 7H), 3.50 (s, 2H), 3.45 – 3.12 (m, 2H), 2.56 (s, 2H), 2.50 – 2.48 (m, 2H), 2.45 (d, J = 5.5 Hz, 6H), 2.43 – 2.33 (m, 1H) 2.08 – 1.79 (m, 3H). (Compound 146)

EXAMPLES FOR COMPARISON

Prepare the following comparison example (as shown in Table 9) essentially as described for Example 7 in WO2018119266.

Table 9

Com. EX. No.	Chemical Name	Structure
1	(2S,2'S)-1,1'-(((2,2'-dimethyl-[1,1'-biphenyl]-3,3'-diyl)bis(6-(cyanomethoxy)benzo[d]oxazole-2,5-diyl))bis(methylene))bis(piperidine-2-carboxylic acid)	

PD-1/PD-L1 BINDING ASSAY (Alphascreen)

The assays were conducted in a standard black 384-well polystyrene plate with a final volume of 20 μL. Inhibitors were first serially diluted in DMSO and then added to the plate wells before the addition of other reaction components. The final concentration of DMSO in the assay was 1%. Add 100 nL/well of compound to the 384 reaction plate (6008280, PerkinElmer) with Echo and centrifuge at 1000 rpm for 1 minute. Add 5 μL/well 4 X PD-L1 solutions to the 384 reaction plate, centrifuge at 1000 rpm for 1 minute, and add 5 μL/well 4 X PD-1 solutions, centrifuge at 1000 rpm for 1 minute, and incubate at 25 °C for 15 minutes. The concentrations of the compounds were 300, 100, 33.33, 11.11, 3.70, 1.23, 0.41, 0.137, 0.046, 0.015, 0 nM, respectively. Add 10 μL/well 2X Anti-6xHis AlphaLISA Acceptor beads and Streptavidin Donor beads solution（PerkinElmer-AL356F） to the above 384 reaction plate, centrifuge at 1000 rpm for 1 minute, and incubate at 25 °C in the dark for 120 minutes. Read the AlphaLISA signal value using the Envision Reader. IC50 determination was performed by fitting the curve of percent control activity versus the log of the inhibitor concentration using the GraphPad Prism 8.0 software.

Compounds of the present disclosure, as exemplified in the Examples, showed IC_{50} values in the following ranges: "*" stands for "0.1nM<IC_{50}≤5nM"; "**" stands for "5nM<IC_{50}≤50nM"; "***" stands for "IC_{50}>50nM".

Data obtained for the Example compounds using the PD-1/PD-L1 binding assay (Alphascreen) described above is provided in Table 10.

Table 10

EX No.	IC_{50}(nM)	EX No.	IC_{50}(nM)	EX No.	IC_{50}(nM)	EX No.	IC_{50}(nM)
1	0.89	80	**	159	*	238	2.3
2	0.2	81	**	160	*	239	0.99
3	89	82	*	161	*	240	**
4	1.4	83	**	162	**	241	**
5	0.4	84	*	163	**	242	*
6	4.3	85	*	164	**	243	2.5
7	0.61	86	11	165	*	244	2

8	0.75	87	*	166	**	245	3.8
9	18	88	*	167	**	246	1.8
10	19	89	*	168	*	247	5.2
11	33	90	0.88	169	*	248	**
12	1.1	91	*	170	**	249	**
13	26	92	*	171	*	250	*
14	1.2	93	*	172	0.3	251	**
15	0.5	94	1.9	173	0.93	252	*
16	1.1	95	1.4	174	21	253	4.7
17	1.2	96	0.6	175	3.4	254	16
18	164	97	*	176	0.9	255	2.3
19	1.3	98	*	177	0.94	256	***
20	1.6	99	0.82	178	3.9	257	4.4
21	0.59	100	*	179	*	258	**
22	25	101	2.2	180	*	259	*
23	7.7	102	18	181	*	260	**
24	0.98	103	0.13	182	*	261	*
25	0.3	104	0.19	183	**	262	**
26	*	105	*	184	2.3	263	0.98
27	0.66	106	*	185	*	264	*
28	3.2	107	*	186	*	265	0.73
29	1.2	108	*	187	*	266	**
30	*	109	1.6	188	*	267	**
31	0.5	110	*	189	*	268	*
32	3.8	111	*	190	0.2	269	**
33	1.5	112	*	191	**	270	**
34	1.3	113	0.5	192	**	271	*
35	0.91	114	1	193	**	272	1.9
36	1.1	115	*	194	**	273	**
37	*	116	*	195	**	274	*
38	*	117	*	196	**	275	**
39	2.4	118	78	197	**	276	*
40	*	119	1.9	198	***	277	*
41	**	120	1.1	199	**	278	*
42	*	121	0.6	200	**	279	*
43	**	122	*	201	***	280	5.7
44	1.1	123	*	202	0.37	281	1.3
45	*	124	*	203	12	282	**

46	**	125	*	204	*	283	**
47	*	126	*	205	*	284	**
48	*	127	3.1	206	1.4	285	*
49	*	128	0.14	207	**	286	*
50	*	129	1.7	208	114	287	*
51	*	130	*	209	1.4	288	1.5
52	*	131	2.3	210	*	289	0.66
53	*	132	2	211	*	290	*
54	6.3	133	*	212	8.4	291	*
55	0.57	134	*	213	**	292	**
56	0.83	135	*	214	***	293	11
57	1.2	136	*	215	2.8	294	*
58	0.79	137	*	216	*	295	**
59	2.5	138	*	217	0.67	296	12
60	*	139	*	218	*	297	26
61	1.6	140	*	219	*	298	**
62	2.6	141	*	220	*	299	***
63	5.7	142	*	221	*	300	***
64	1.8	143	*	222	*	301	**
65	1.3	144	*	223	*	302	0.29
66	1.8	145	*	224	*	303	1.6
67	6.7	146	*	225	2	304	27
68	2.4	147	*	226	4.7	305	0.87
69	0.49	148	**	227	4.1	306	1.5
70	3.3	149	*	228	4.3	307	*
71	0.37	150	*	229	6.9	308	*
72	0.98	151	*	230	1.5	309	*
73	0.42	152	*	231	78	310	*
74	1.1	153	*	232	7.8	311	*
75	10	154	**	233	41	312	*
76	32	155	*	234	0.52	313	*
77	1.2	156	*	235	1.8	314	8
78	*	157	*	236	290	315	*
79	*	158	*	237	2.7	316	**

Pharmacokinetic Assay

Adult C57 female mice were received to single-dose of the test compounds with 10% DMSO, 10% Kolliphor@HS 15 and 80% saline as excipients, the mice (n=9) were giving oral

administration (intragastric administration) with the compounds at a dose of 100 mg/kg. Time of blood collection: 15 min, 30 min, 1 h, 2 h, 4 h, 7 h, 24 h. Approximately 0.1 mL of whole blood was collected from retro-orbital venous plexus of 3 mice at each time point, and placed into tubes that contained K_2-EDTA as an anticoagulant. The whole blood was centrifuged at 4°C and 4000 rpm for 10 min. The plasma was transferred into centrifuge tubes, and stored at -20°C untill being analyzed. Concentrations of test compounds in the plasma samples were analyzed with liquid chromatography-tandem mass spectrometry (LC-MS/MS). Plasma concentration-time data of individual animals was analyzed using Microsoft Excel 2010. Non-compartmental model was introduced in concentration analysis. The pharmacokinetic parameters of the test compounds were calculated using WinNonlin (version 4.1; Pharsight) software. The data is shown in Table 11.

Adult C57 female mice were received to single-dose of the test compounds with 15% DMSO, 10% Kolliphor@HS 15 and 75% saline as excipients, the mice (n=3) were giving oral administration (intragastric administration) with the compounds at a dose of 5 mg/kg. Time of blood collection: 30 min, 2 h, 4 h. approximately 0.1 mL of whole blood was collected from retro-orbital venous plexus, and placed into tubes that contained K_2-EDTA as an anticoagulant. The whole blood were centrifuged at 4°C and 4000 rpm for 10 min. The plasma was transferred into centrifuge tubes, and stored at -20°C untill being analyzed. Concentrations of test compounds in the plasma samples were analyzed with liquid chromatography-tandem mass spectrometry (LC-MS/MS). Plasma concentration-time data of individual animals was analyzed using Microsoft Excel 2010. The data is shown in Table 12.

Table 11

EX No.	Dose (mg/kg)	$T_{1/2}$(hr)	T_{max}(hr)	C_{max} (ng/mL)	AUC (hr*ng/mL)
Com. EX. No.1	100	1.94	1	76	196
2	100	3.30	0.5	218	271
3	100	0.39	1	374	461
5	100	5.07	4	2597	25686
8	100	3.97	4	974	8243
12	100	7.97	2	1383	14536
14	100	6.20	1	589	3453
15	100	9.83	1	931	5711
16	100	4.80	4	1473	20947
95	100	6.48	4	2033	22866
98	100	4.47	1	1007	8699
28	100	2.79	1	1283	5805

29	100	4.67	1	3720	42711
108	100	21.7	1	713	10139
31	100	9.81	1	1003	6605
33	100	11.00	4	727	8915
34	100	6.99	4	4257	56146
36	100	8.26	1	1667	21381
61	100	5.37	4	8653	117700
62	100	9.69	4	4280	46470
63	100	5.80	1	2923	43669
64	100	7.20	7	4317	61468
65		10.74	4	2457	40371
100	100	10.5	4	18900	235468
171	100	3.66	1	965	3474
175	100	3.63	2	1627	19943
314	100	5.43	2	6353	28971
190	100	3.57	1	1280	8572
243	100	6.93	1	4887	67353
244	100	7.01	2	5737	78121
88	100	NA	24	117333	2024036
74	100	8.20	4	4463	59508
93	100	NA	4	9217	162649
103	100	23.40	4	5587	96382

Table 12

EX No.	**Dose (mg/kg)**	**Concentration (ng/mL)**		
		0.5h	**2h**	**4h**
Com. EX. No.1	5.0	NA	NA	NA
5	5.0	43.9	55.7	61.2
10	5.0	80.9	221	214
13	5.0	79.3	241	301
18	5.0	303	642	626
22	5.0	68.6	155	81.1
23	5.0	46.2	148	94.7
34	5.0	46.8	136	154
56	5.0	19.9	192	155
57	5.0	27.1	149	90.0
66	5.0	NA	137	111

67	5.0	143	418	462
70	5.0	36.4	151	158
72	5.0	42.6	140	132
80	5.0	247	299	167
81	5.0	115	468	383
85	5.0	75.9	146	135
89	5.0	21.3	124	109
101	5.0	178	640	579
102	5.0	85.9	282	292
103	5.0	48.9	185	135
114	5.0	65.6	237	152
117	5.0	121	319	243
127	5.0	61.3	253	216
131	5.0	108	301	470
136	5.0	673	736	545
142	5.0	211	243	171
144	5.0	243	386	222
162	5.0	277	670	441
164	5.0	294	877	853
165	5.0	376	404	219
191	5.0	520	1167	1333
192	5.0	469	440	268
195	5.0	256	255	125
197	5.0	527	741	369
198	5.0	674	1440	1097
201	5.0	428	792	527
203	5.0	819	1026	833
204	5.0	740	872	820
205	5.0	1002	1437	1420
209	5.0	21.4	54.9	19.2
227	5.0	36.9	149	114
231	5.0	36.9	160	156
233	5.0	143	322	296
237	5.0	58.5	178	186
241	5.0	102	234	294
242	5.0	90.4	223	202
245	5.0	101	237	191
246	5.0	87.2	261	285

248	5.0	89.0	271	369
252	5.0	694	2873	4153
253	5.0	42.3	199	181
272	5.0	66.1	198	141
276	5.0	131	291	238
280	5.0	33.6	171	113
283	5.0	522	1173	965
285	5.0	39.1	80.0	41.8
286	5.0	20.5	73.8	52.2
288	5.0	8.36	25.4	9.68
293	5.0	6.68	10.8	3.57
294	5.0	80.4	193	186
299	5.0	27.9	212	89.2
304	5.0	131	150	74.2
317	5.0	20.6	88.5	44.3

NA = not applicable

As shown in Table 11 and Table 12, we can see, the exemplified compounds of the present invention display unexpectedly better pharmacokinetic properties than the known compounds, Com. EX. No.1.

NFAT assay

PD-1 / PD-L1 Blockade Bioassay contains two cells: PD-1 Effector Cells, which are the Jurkat T cells expressing hPD-1 and luciferase reporter genes; PD-L1 aAPC / CHO-K1 Cells, which are the CHO-K1 cells expressing hPD-L1 and activate TCR's cell surface proteins. The antibody or small molecule compound is incubated with these two cells for a period of time, and the amount of the product is detected using Bio-Glo Luciferase reagent and chemiluminescence method to reflect the influence of antibody or small molecule compound on PD-1 / PD-L1 interaction.

Assay buffer: 49.5 mL RPMI-1640; 0.5 mL FBS

Cell medium: 36 mL Ham's F-12; 4 mL FBS

Reaction process:

1) Resuscitate PD-L1 aAPC / CHO-K1 Cells on the first day and the cells were suspended and counted with cell recovery medium. The cells were diluted to 2.65 * 10^5 / ml with cell medium. Seed cells at density of 6000 cells/well of 384-wells plates, incubator for 16-24 h;

2) Dilute the compound to 5 mM with DMSO. The 5mM solution was used as the first concentration, and a 3-fold gradient dilution was performed, with a total of 9 concentration gradients, and the 10th concentration was used as the DMSO control;

3) Positive control antibody Atezolizumab was diluted to 4 μg/ml with assay buffer. 4 μg / ml was used as the first concentration, and a 2.5-fold gradient dilution was performed, with a total of 9 concentration gradients, and the 10th concentration was used as the assay buffer control;

4) Aspirate the medium from the 384-well plate. Add 10 μL / well of compound to the 384-well plate and incubate for 2 hours;

5) Resuscitate PD-1 effector cells and the cells were suspended and counted with cell recovery medium. The cells were diluted to $8.75*10^5$ / ml with cell medium. Seed cells at density of 8000 cells/well to 384-wells plates of step4, incubator for 17 h;

6) Add 20 μL/well of Bio-Glo luciferase reagent to the 384 reaction plate of step 5, and incubate at 25 °C for 5-30 minutes.

7) Read the RLU (relative luminescence unit) value using the Envision multi-plate reader. The experimental data were plotted using compound concentration as X value and RLU as Y value.

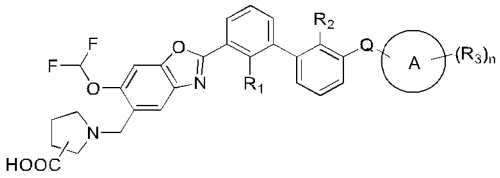
The results are expressed as EC_{50} value which is provided in Table 13.

Table 13

EX No.	EC_{50}(nM)
5	317
103	254
317	4697
318	3225

THE CLAIMS:

1. A compound of Formula (I), or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof,



Formula (I)

Wherein,

R_1 and R_2 are each independently selected from halogen, CN, C_{1-6} alkyl, or C_{1-4} haloalkyl;

Q is a bond, -NH-, or $-(CH_2)_m-O-$;

Ring A is C_{5-6} aryl , C_{5-6} heteroaryl, C_{4-6} cycloalkyl or C_{4-6} heterocycloalkyl, wherein the C_{5-6} heteroaryl and C_{4-6} heterocycloalkyl optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O; or

Ring A is C_{8-10} fused bicyclic ring;

R_3 is H, halogen, $-(CH_2)_s-NR_4R_5$, C_{1-4} alkyl, C_{1-4} alkoxyl, hydroxyl, oxo, CN, $(CH_2)_q-CONR_4R_5$, $-COR_4$, $-NR_4R_5$, $-NR_4C(=O)NR_4R_5$, $-NR_4C(=NR_4)NR_4R_5$, $-S(O)_2R_4$, $-S(O)_2NR_4R_5$, $-S(O)R_4$, $-S(O)NR_4R_5$, C_{2-6} alkenyl, C_{2-6} alknyl , C_{1-6} haloalkyl, C_{5-6} aryl, C_{5-6} heteroaryl, C_{3-6} cycloalkyl or C_{3-6} heterocycloalkyl, wherein the C_{5-6} heteroaryl and C_{3-6} heterocycloalkyl optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O; the C_{1-4} alkyl, C_{1-4} alkoxyl, C_{2-6} alkenyl, C_{2-6} alknyl, C_{1-6} haloalkyl, C_{5-6} aryl , C_{5-6} heteroaryl, C_{3-6} cycloalkyl and C_{3-6} heterocycloalkyl optionally substituted with one or more substitutents independently selected R_6 substituents;

R_4 and R_5 are each independently selected from H, C_{1-4} alkyl, or C_{3-6} cycloalkyl, C_{3-6} heterocyclyl, the C_{1-4} alkyl, C_{3-6} cycloalkyl, or C_{3-6} heterocyclyl optionally substituted with one or more substitutents independently selected R_6 substituents; or

R_4 and R_5 together with the atoms to which they are attached form a 4-10-member heterocyclic ring optionally substituted with one or more substituents independently selected R_6 substituents;

R_6 is H, halogen, hydroxyl, oxo, CN, $-(CH_2)_k-NR_7R_8$, $-COR_7$, $-NR_7R_8$, $-NR_7C(=O)NR_7R_8$, $-NR_7C(=NR_7)NR_7R_8$, $-S(O)_2R_7$, $-S(O)_2NR_7R_8$, $-S(O)R_7$, $-S(O)NR_7R_8$, or R_6 is selected from substituted or unsubstituted C_{1-4} alkyl, C_{1-4} alkoxyl, C_{2-6} alkenyl, C_{2-6} alknyl, C_{1-6} haloalkyl, C_{5-6} aryl , C_{5-6} heteroaryl, C_{3-10} heterocyclic ring, wherein the C_{5-6} heteroaryl and C_{3-10} heterocyclic ring optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O;

R_7 and R_8 are each independently selected from H, halogen, hydroxyl, oxo, CN, -$S(O)_2$- C_{1-4} alkyl, -NH_2, -NH- C_{1-4} alkyl, -(CH_2)-$N(C_{1-4}$ alkyl$)_2$, or R_7 and R_8 are each independently selected from substituted or unsubstituted C_{1-4} alkyl, C_{1-4} alkoxyl, C_{2-6} alkenyl, C_{2-6} alknyl , C_{1-6} haloalkyl, C_{5-6} aryl , C_{5-6} heteroaryl, C_{3-6} cycloalkyl, C_{3-6} heterocycloalkyl; wherein the C_{5-6} heteroaryl and C_{3-6} heterocycloalkyl optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O;

m, n, q, k and s are each independently selected from 0, 1, 2, 3 or 4.

2. The compound of claim 1, or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein,

R_3 is H, halogen, -$(CH_2)_s$-NR_4R_5, C_{1-4} alkyl, C_{1-4} alkoxyl, hydroxyl, oxo, CN, $(CH_2)_q$-$CONR_4R_5$, -NR_4R_5, -$NR_4C(=NR_4)NR_4R_5$, -$S(O)_2R_4$, C_{2-6} alkenyl, C_{2-6} alknyl, C_{1-6} haloalkyl or C_{3-6} heterocycloalkyl, wherein the C_{3-6} heterocycloalkyl optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O; the C_{1-4} alkyl, C_{1-4} alkoxyl, C_{2-6} alkenyl, C_{2-6} alknyl , C_{1-6} haloalkyl, and C_{3-6} heterocycloalkyl optionally substituted with one or more substitutents independently selected R_6 substituents.

3. The compound of claim 1, or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein,

R_3 is H, halogen, -$(CH_2)_s$-NR_4R_5, -CN, -$S(O)_2R_4$, C_{1-4} alkyl, C_{1-4} alkoxyl, the -$(CH_2)_s$-NR_4R_5, C_{1-4} alkyl, C_{1-4} alkoxyl optionally substituted with one or more substitutents independently selected R_6 substituents.

4. The compound of any one of claims 1-3, or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein,

R_6 is H, halogen, hydroxyl, oxo, CN, -$(CH_2)_k$ -NR_7R_8, -COR_7, -NR_7R_8, -$NR_7C(=O)NR_7R_8$, -$S(O)_2R_7$ or R_6 is selected from substituted or unsubstituted C_{1-4} alkyl, C_{1-4} alkoxyl, C_{2-6} alkenyl, C_{2-6} alknyl, C_{1-6} haloalkyl, C_{5-6} aryl, C_{5-6} heteroaryl, C_{3-10} heterocyclic ring, wherein the C_{5-6} heteroaryl and C_{3-10} heterocyclic ring optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O.

5. The compound of any one of claims 1-3, or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein,

R_6 is H, halogen, hydroxyl, oxo, CN, -(CH_2) -N-$(C_{1-4}$ alkyl$)_2$, -(CH_2)-NH2, -N-$(C_{1-4}$ alkyl$)_2$,-NH_2, -CO-N-$(C_{1-4}$ alkyl$)_2$, -CO-NH_2,- $S(O)_2$-C_{1-4} alkyl, C_{1-4} alkyl-OH, C_{1-4} alkyl, C_{1-4} alkoxyl, C_{2-6} alkenyl, C_{2-6} alknyl, C_{1-6} haloalkyl, C_{5-6} aryl, C_{5-6} heteroaryl, C_{3-10} heterocyclic ring, wherein the C_{5-6} heteroaryl and C_{3-10} heterocyclic ring optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O.

6. The compound of any one of claims 1-3, or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein,

R_6 is halogen, oxo, -OH, $-NH_2$, $-N(CH_3)_2$, $-C_{1-4}$ alkyl-OH, $-C_{1-4}$ alkyl-NH-CH_3, -NH-C_{1-4} alkyl, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxyl, C_{5-6} aryl, C_{5-6} heteroaryl, C_{3-6} heterocyclyl, guanidine, or sulfone.

7. The compound of claim 1, or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein,

R_1 and R_2 are each independently selected from halogen, CN, $-C_{1-6}$alkyl, or $-C_{1-4}$ haloalkyl;

Q is a bond, -NH-, or $-(CH_2)_m$-O-;

ring A is C_{5-6} aryl or C_{5-6} heteroaryl ring, wherein the C_{5-6} heteroaryl ring optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O; or

ring A is C_{8-10} fused bicyclic ring;

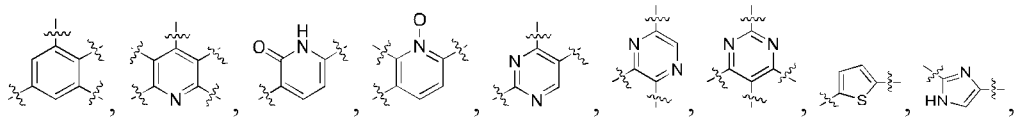
R_3 is H, halogen, $-(CH_2)_s$-NR_4R_5, $-C_{1-4}$ alkyl, $-C_{1-4}$ alkoxyl, the $-(CH_2)_s$-NR_4R_5, $-C_{1-4}$ alkyl, $-C_{1-4}$ alkoxyl optionally substituted with one or more substitutents independently selected from halogen, $-C_{1-4}$ alkyl, $-C_{1-4}$ haloalkyl, $-C_{1-4}$ alkoxyl, C_{5-6} heteroaryl, C_{5-6} aryl, carboxyl, amino, hydroxyl, guanidine, or sulfone;

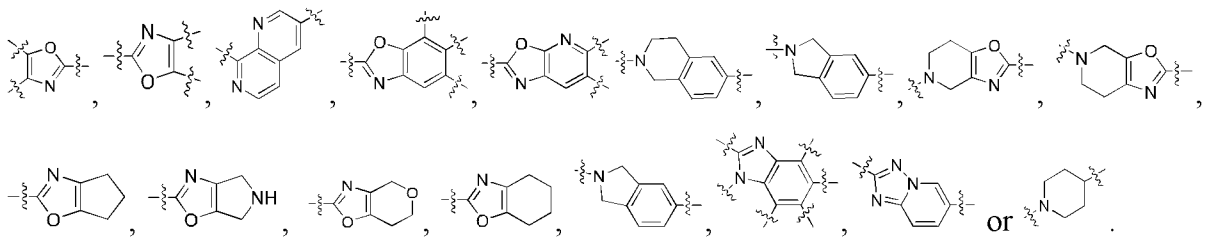
R_4 and R_5 are each independently selected from H, $-C_{1-4}$ alkyl, or C_{3-6} cycloalkyl, C_{3-6} heterocyclyl, the $-C_{1-4}$ alkyl, or C_{3-6} cycloalkyl, C_{3-6} heterocyclyl optionally substituted with halogen, -OH, $N(CH_3)_2$, $-C_{1-4}$ alkyl, $-C_{1-4}$ haloalkyl, $-C_{3-6}$ heterocyclyl, -NH-C_{1-4} alkyl, or sulfone; or

R_4 and R_5 together with the atoms to which they are attached form a 4- to 6-member heterocyclic ring optionally substituted with one or more substituents independently selected from -OH, $-N(CH_3)_2$, $-NH_2$, oxo, halogen, $-C_{1-4}$ alkyl, $-C_{1-4}$ alkoxyl, $-C_{1-4}$ alkyl-OH, $-C_{1-4}$ alkyl-NH-CH_3, or sulfone;

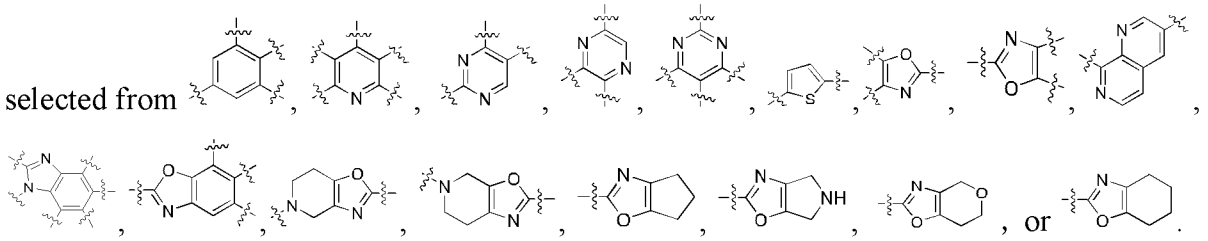
m, n and s are each independently selected from 0, 1, 2, 3 or 4.

8. The compound of any one of claims 1-7, or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein Q is selected from bond, -NH- or-CH_2-O-.

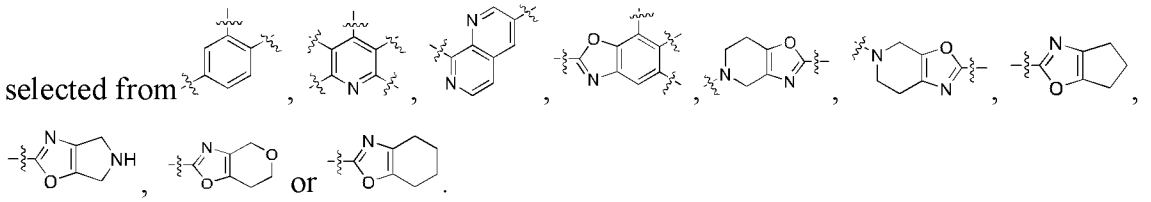
9. The compound of any one of claims 1-8, or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein ring A is selected from  ,



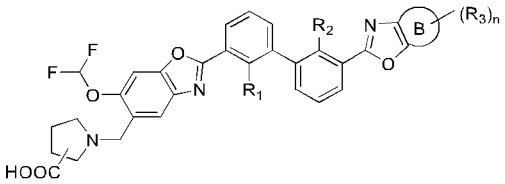
10. The compound of any one of claims 1-8, or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein ring A is selected from



11. The compound of any one of claims 1-8, or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein ring A is selected from



12. The compound of any one of claims 1-7, or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein the compound having Formula(II):

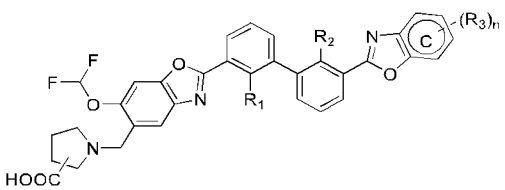


Formula (II)

or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein,

ring B is C_{5-6} cycloalkyl or C_{5-6} heterocycloalkyl.

13. The compound of any one of claims 1-7, wherein the compound having Formula(III):

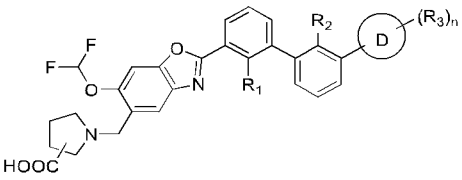


Formula (III)

or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein,

ring C is phenyl or heteroaryl, and the heteroaryl comprising 1, 2 or 3 N.

14. The compound of any one of claims 1-7, wherein the compound having Formula(IV):

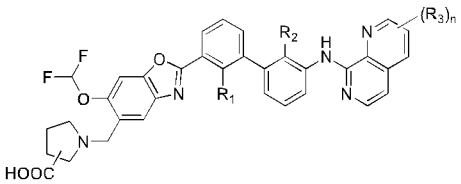


Formula (IV)

or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein,

ring D is C_{5-6} aryl, C_{5-6} heteroaryl, or C_{5-6} heterocycloalkyl, and the C_{5-6} heteroaryl and C_{5-6} heterocycloalkyl optionally comprising 1, 2 or 3 hetero atoms independently selected from N, S, or O.

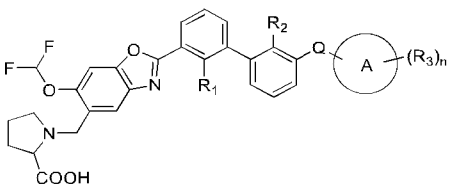
15. The compound of any one of claims 1-7, wherein the compound having Formula(V):



Formula (V)

or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof.

16. The compound of any one of claims 1-11, wherein the compound having Formula(VI):



Formula (VI)

or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof.

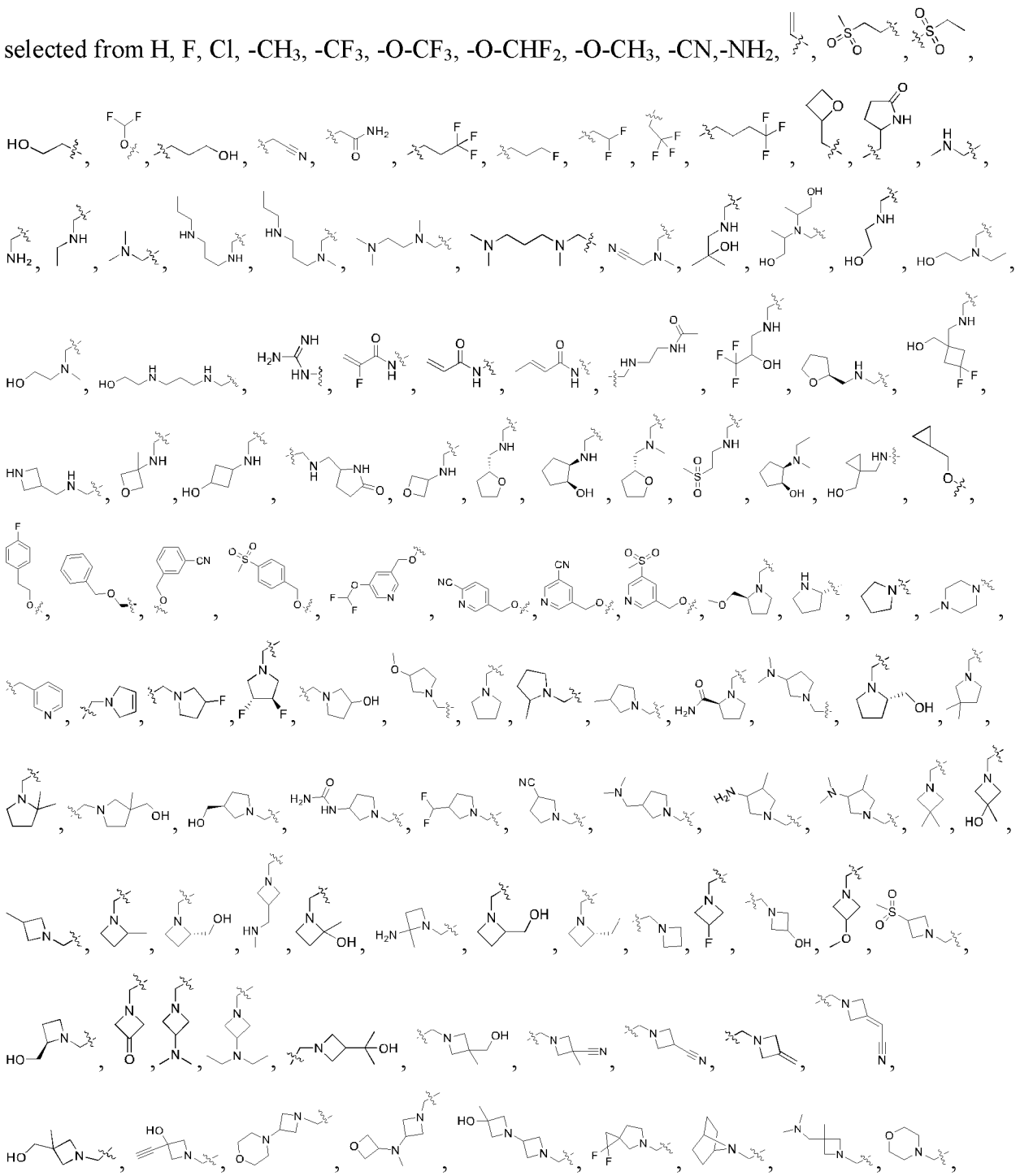
17. The compound of any one of claims 1-16, or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein R_1 is selected from F, Cl, $-CH_3$, -CN or $-O-CH_3$.

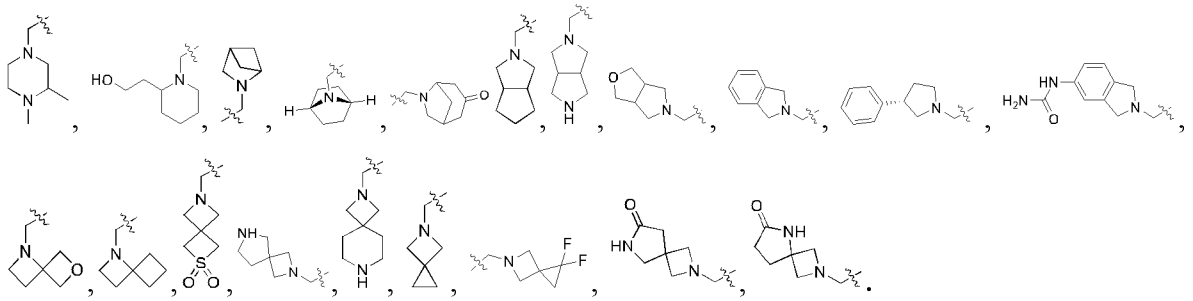
18. The compound of any one of claims 1-17, or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein R_1 is selected from $-CH_3$, F, or $-O-CH_3$.

19. The compound of any one of claims 1-18, or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein R_2 is selected from $-CH_3$, F, Cl, or Br.

20. The compound of any one of claims 1-19, or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein R_2 is $-CH_3$.

21. The compound of any one of claims 1-20, or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein R_3 is selected from H, F, Cl, $-CH_3$, $-CF_3$, $-O-CF_3$, $-O-CHF_2$, $-O-CH_3$, $-CN$, $-NH_2$,





22. The compound of any one of claims 1-21, or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein s is 1.

23. The compound of any one of claims 1-21, or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein m is 1.

24. The compound of claim 1, or a stereoisomer, tautomer, pharmaceutically acceptable salt, prodrug, chelate, non-covalent complex, or solvate thereof, wherein the compound is:

1) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((((1R,2S)-2-hydroxycyclopentyl)(methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

2) (2'S)-(((2,2'-dimethyl-[1,1'-biphenyl]-3,3'-diyl)bis(6-(difluoromethoxy)benzo[d]oxazole-2,5-diyl))bis(methylene))di-L-proline;

3) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((S)-2-(methoxycarbonyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

4) ((2-(2'-cyano-3'-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

5) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

6) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2'-fluoro-2-methyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

7) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((2-hydroxyethyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

8) ((2-(3'-(5-(azetidin-1-ylmethyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

9) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-fluoroazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

10) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-fluoropyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

11) ((2-(3'-(5-(((S)-2-carbamoylpyrrolidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

12) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((S)-2-(hydroxymethyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

13) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(morpholinomethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

14) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-hydroxypyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

15) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((methylamino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

16) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((dimethylamino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

17) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((2-hydroxyethyl)(methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

18) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((3R,4R)-3,4-difluoropyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

19) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((((S)-5-oxopyrrolidin-2-yl)methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

20) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-hydroxyazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

21) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((ethylamino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

22) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((3,3,3-trifluoro-2-hydroxypropyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

23) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3,4-dimethylpiperazin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

24) ((2-(3'-(5-(aminomethyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

25) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((((1R,2S)-2-hydroxycyclopentyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

26) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((((1R,2S)-2-hydroxycyclopentyl)(methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-D-proline;

27) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((((1S,2R)-2-hydroxycyclopentyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

28) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((oxetan-3-ylamino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

29) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((((R)-tetrahydrofuran-2-yl)methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

30) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((methyl(((R)-tetrahydrofuran-2-yl)methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

31) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((S)-2-(hydroxymethyl)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

32) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((2-(methylsulfonyl)ethyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

33) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-(dimethylamino)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

34) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

35) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((R)-2-(hydroxymethyl)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

36) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((2-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

37) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((2-hydroxy-2-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

38) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((2-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

39) ((2-(3'-(5-((6-oxa-1-azaspiro[3.3]heptan-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

40) ((2-(3'-(5-((2-amino-2-methylazetidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

41) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-(methylsulfonyl)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

42) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((R)-2-ethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

43) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-methoxyazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

44) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-hydroxy-3-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

45) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-((methylamino)methyl)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

46) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-oxoazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

47) ((2-(3'-(5-((2-oxa-6-azaspiro[3.3]heptan-6-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

48) ((2-(3'-(5-((2-azaspiro[3.3]heptan-2-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

49) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((hexahydrocyclopenta[c]pyrrol-2(1H)-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

50) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

51) ((2-(3'-(5-((2,7-diazaspiro[3.5]nonan-2-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

52) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((3-(propylamino)propyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

53) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((methyl(3-(propylamino)propyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

54) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((2,2-dioxido-2-thia-6-azaspiro[3.3]heptan-6-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

55) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((tetrahydro-1H-furo[3,4-c]pyrrol-5(3H)-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

56) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

57) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((((1R,2R)-2-hydroxycyclopentyl)(methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

58) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((3-((2-hydroxyethyl)amino)propyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

59) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((2-(dimethylamino)ethyl)(methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

60) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((2-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

61) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

62) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((2,2-dimethylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

63) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((S)-2-(methoxymethyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

64) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(((((S)-tetrahydrofuran-2-yl)methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

65) ((2-(2'-cyano-3'-(6-(difluoromethoxy)-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline;

66) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-D-proline;

67) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3,3-dimethylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

68) ((2-(3'-(5-((3-(diethylamino)azetidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

69) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-(2-hydroxypropan-2-yl)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

70) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((2,5-dihydro-1H-pyrrol-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

71) ((2-(3'-(5-((2-azabicyclo[2.1.1]hexan-2-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

72) ((2-(3'-(5-(((1s,4s)-7-azabicyclo[2.2.1]heptan-7-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

73) ((2-(3'-(5-((((3,3-difluoro-1-(hydroxymethyl)cyclobutyl)methyl)amino)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

74) ((2-(3'-(5-((5-azaspiro[2.3]hexan-5-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

75) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-oxo-6-azabicyclo[3.2.1]octan-6-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

76) ((2-(3'-(5-((1,1-difluoro-5-azaspiro[2.3]hexan-5-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

77) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-(hydroxymethyl)-3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

78) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-(hydroxymethyl)-3-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

79) ((2-(3'-(5-((3-cyano-3-methylazetidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

80) ((2-(3'-(5-((3-cyanoazetidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

81) ((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3-methyleneazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

82) ((2-(3'-(5-((3-(cyanomethylene)azetidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

83) ((2-(2,2'-dicyano-3'-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

84) ((6-(difluoromethoxy)-2-(3'-(5-((3,4-dimethylpyrrolidin-1-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

85) (R)-1-((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid;

86) (S)-1-((6-(difluoromethoxy)-2-(3'-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid;

87) ((2-(2'-cyano-3'-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline;

88) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((3-methylpyrrolidin-1-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

89) ((2-(3'-(5-((2-azabicyclo[2.1.1]hexan-2-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

90) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((3-methylpyrrolidin-1-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-D-proline;

91) (3R)-1-((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((3-methylpyrrolidin-1-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid;

92) (3S)-1-((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((3-methylpyrrolidin-1-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid;

93) ((6-(difluoromethoxy)-2-(3'-(5-((3,3-dimethylazetidin-1-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

94) ((2-(3'-(5-(azetidin-1-ylmethyl)-7-methylbenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

95) ((6-(difluoromethoxy)-2-(3'-(7-fluoro-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

96) ((6-(difluoromethoxy)-2-(3'-(5-((ethylamino)methyl)-6-fluorobenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

97) ((2-(3'-(6-chloro-5-((ethylamino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

98) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

99) ((6-(difluoromethoxy)-2-(3'-(5-((((1R,2S)-2-hydroxycyclopentyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

100) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

101) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)-6-(trifluoromethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

102) ((2-(3'-(6,7-difluoro-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

103) ((2-(3'-(7-cyano-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

104) ((6-(difluoromethoxy)-2-(3'-(5-((2-hydroxy-2-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

105) ((6-(difluoromethoxy)-2-(3'-(5-((2-(hydroxymethyl)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

106) ((2-(3'-(5-((6-oxa-1-azaspiro[3.3]heptan-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

107) ((2-(3'-(5-((1-azaspiro[3.3]heptan-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

108) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(6-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

109) ((6-(difluoromethoxy)-2-(3'-(6-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

110) ((2-(2'-chloro-3'-(6-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

111) ((2-(2'-chloro-3'-(6-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline;

112) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(6-(pyrrolidin-1-ylmethyl)oxazolo[5,4-b]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

113) ((6-(difluoromethoxy)-2-(3'-(6-((3,3-dimethylazetidin-1-yl)methyl)oxazolo[5,4-b]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

114) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(6-(((R)-3-methylpyrrolidin-1-yl)methyl)oxazolo[5,4-b]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

115) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(6-((((5-oxopyrrolidin-2-yl)methyl)amino)methyl)oxazolo[5,4-b]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

116) ((6-(difluoromethoxy)-2-(3'-(6-((3-(dimethylamino)azetidin-1-yl)methyl)oxazolo[5,4-b]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

117) ((2-(3'-(6,7-difluoro-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2'-methoxy-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

118) ((2-(2'-cyano-3'-(6,7-difluoro-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

119) ((2-(3'-(6-((6-cyanopyridin-3-yl)methoxy)-5-(((2-hydroxyethyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

120) ((2-(3'-(6-((5-cyanopyridin-3-yl)methoxy)-5-(((2-hydroxyethyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

121) ((6-(difluoromethoxy)-2-(3'-(5-(((2-hydroxyethyl)amino)methyl)-6-((5-(methylsulfonyl)pyridin-3-yl)methoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

122) ((6-(difluoromethoxy)-2-(3'-(5-((ethylamino)methyl)-6-((5-(methylsulfonyl)pyridin-3-yl)methoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

123) ((6-(difluoromethoxy)-2-(3'-(5-((dimethylamino)methyl)-6-((5-(methylsulfonyl)pyridin-3-yl)methoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

124) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((methylamino)methyl)-6-((3-(methylsulfonyl)benzyl)oxy)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

125) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((methylamino)methyl)-6-((4-(methylsulfonyl)benzyl)oxy)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

126) ((6-(difluoromethoxy)-2-(3'-(5-((dimethylamino)methyl)-6-((4-(methylsulfonyl)benzyl)oxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

127) ((2-(3'-(7-cyano-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

128) ((2-(2-cyano-3'-(6-(difluoromethoxy)-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2'-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

129) ((2-(3'-(7-cyano-5-((3-(hydroxymethyl)-3-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

130) ((2-(3'-(7-cyano-5-(((S)-3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

131) ((2-(3'-(7-cyano-5-(((R)-3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

132) ((2-(3'-(7-cyano-5-(((R)-3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline;

133) ((2-(3'-(7-cyano-5-(((3-methyloxetan-3-yl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

134) ((2-(3'-(7-cyano-5-((3-(dimethylamino)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

135) ((2-(3'-(7-cyano-5-((2-(2-hydroxyethyl)piperidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

136) ((2-(3'-(7-cyano-5-(((cyanomethyl)(methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

137) ((2-(3'-(7-cyano-5-((3-(hydroxymethyl)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

138) ((2-(3'-(7-cyano-5-(((2-hydroxy-2-methylpropyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

139) ((2-(3'-(7-cyano-5-((((5-oxopyrrolidin-2-yl)methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

140) ((2-(3'-(7-cyano-5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline;

141) ((2-(3'-(7-cyano-5-((ethyl(2-hydroxyethyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

142) ((2-(3'-(7-cyano-5-((3-cyanopyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

143) ((2-(3'-(7-cyano-5-((3-cyanopyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline;

144) ((2-(3'-(7-cyano-5-((3-ethynyl-3-hydroxyazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

145) ((2-(3'-(7-cyano-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline;

146) ((2-(3'-(7-cyano-5-((7-oxo-2,6-diazaspiro[3.4]octan-2-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

147) ((2-(3'-(5-((bis(1-hydroxypropan-2-yl)amino)methyl)-7-cyanobenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

148) ((2-(3'-(7-cyano-5-((3-morpholinoazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

149) ((2-(3'-(7-cyano-5-((3-(methyl(oxetan-3-yl)amino)azetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

150) ((2-(3'-(7-cyano-5-((3-hydroxy-3-methyl-[1,3'-biazetidin]-1'-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

151) ((2-(3'-(7-cyano-5-((6-oxo-2,5-diazaspiro[3.4]octan-2-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

152) ((2-(3'-(7-cyano-5-((3-((dimethylamino)methyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

153) ((2-(3'-(7-cyano-5-((1,1-difluoro-5-azaspiro[2.4]heptan-5-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

154) ((2-(3'-(7-cyano-5-(((R)-3-(hydroxymethyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

155) ((2-(3'-(7-cyano-5-(((3-hydroxycyclobutyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

156) ((2-(3'-(5-((3-amino-4-methylpyrrolidin-1-yl)methyl)-7-cyanobenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

157) ((2-(3'-(5-(((azetidin-3-ylmethyl)amino)methyl)-7-cyanobenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

158) ((2-(3'-(7-cyano-5-((3-(dimethylamino)-4-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

159) ((2-(3'-(7-cyano-5-((3-((dimethylamino)methyl)-3-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

160) ((2-(3'-(7-cyano-5-((((1-methyl-1H-imidazol-4-yl)methyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

161) ((2-(3'-(5-((3-(aminomethyl)-3-methylazetidin-1-yl)methyl)-7-cyanobenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

162) ((2-(3'-(7-cyano-5-((3-fluoropyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

163) ((2-(3'-(7-cyano-5-((3-fluoropyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline;

164) ((2-(3'-(7-cyano-5-((3,4-difluoropyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

165) ((2-(3'-(7-cyano-5-(((R)-3-cyanopyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

166) ((6-(difluoromethoxy)-2-(3'-(5-((3-fluoropyrrolidin-1-yl)methyl)-7-(trifluoromethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

167) ((2-(3'-(7-cyano-5-((3-fluoro-3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

168) ((2-(3'-(7-cyano-5-(((R)-3-(fluoromethyl)pyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

169) (R)-1-((2-(3'-(7-cyano-5-(pyrrolidin-1-ylmethyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid;

170) ((6-(difluoromethoxy)-2-(3'-(6-((3,3-dimethylazetidin-1-yl)methyl)oxazolo[5,4-b]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-D-proline;

171) S)-1-((8-((3'-(5-(((S)-2-carboxypyrrolidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)amino)-1,7-naphthyridin-3-yl)methyl)-2-methylpyrrolidine-2-carboxylic acid;

172) ((2-(3'-((3-(((carboxymethyl)amino)methyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

173) (S)-1-((8-((3'-(5-(((S)-2-carboxypyrrolidin-1-yl)methyl)-6-(difluoromethoxy)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)amino)-1,7-naphthyridin-3-yl)methyl)piperidine-2-carboxylic acid;

174) ((6-(difluoromethoxy)-2-(3'-((3-((3-fluoropyrrolidin-1-yl)methyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

175) ((6-(difluoromethoxy)-2-(3'-((3-((3-hydroxypyrrolidin-1-yl)methyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

176) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-((3-(morpholinomethyl)-1,7-naphthyridin-8-yl)amino)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

177) ((2-(3'-((3-(azetidin-1-ylmethyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline;

178) ((6-(difluoromethoxy)-2-(3'-((3-((3-hydroxyazetidin-1-yl)methyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

179) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-((3-((((5-oxopyrrolidin-2-yl)methyl)amino)methyl)-1,7-naphthyridin-8-yl)amino)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

180) (3S)-1-((6-(difluoromethoxy)-2-(3'-((3-((3-hydroxypyrrolidin-1-yl)methyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid;

181) (3R)-1-((6-(difluoromethoxy)-2-(3'-((3-((3-hydroxypyrrolidin-1-yl)methyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid;

182) ((6-(difluoromethoxy)-2-(3'-((3-((3-hydroxypyrrolidin-1-yl)methyl)-1,7-naphthyridin-8-yl)amino)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-D-proline;

183) ((5-(difluoromethoxy)-2-(2,2'-dimethyl-3'-((4-(pyrrolidin-1-ylmethyl)pyridin-2-yl)amino)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-6-yl)methyl)-L-proline;

184) ((2-(3'-(5-(carboxymethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

185) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(2-(methylsulfonyl)ethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

186) ((2-(3'-(5-(1-carboxyethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

187) ((2-(3'-(5-(2-carboxyethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

188) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-methyl-4,5,6,7-tetrahydrooxazolo[5,4-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

189) ((6-(difluoromethoxy)-2-(3'-(5-(2-hydroxyethyl)-4,5,6,7-tetrahydrooxazolo[5,4-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

190) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

191) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(4,4,4-trifluorobutyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

192) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(oxetan-2-ylmethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

193) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((5-oxopyrrolidin-2-yl)methyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

194) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyridin-3-ylmethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

195) ((2-(3'-(5-(cyanomethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline;

196) ((2-(3'-(5-(2-amino-2-oxoethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline;

197) ((6-(difluoromethoxy)-2-(3'-(5-(ethylsulfonyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

198) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(3,3,3-trifluoropropyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

199) ((6-(difluoromethoxy)-2-(3'-(5-(3-hydroxypropyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

200) ((6-(difluoromethoxy)-2-(3'-(5-(3-fluoropropyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

201) ((2-(3'-(5-(2,2-difluoroethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline;

202) ((6-(difluoromethoxy)-2-(3'-(5,6-dihydro-4H-pyrrolo[3,4-d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

203) ((6-(difluoromethoxy)-2-(3'-(6,7-dihydro-4H-pyrano[3,4-d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

204) ((6-(difluoromethoxy)-2-(3'-(5,6-dihydro-4H-cyclopenta[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

205) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(4,5,6,7-tetrahydrobenzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

206) ((6-(difluoromethoxy)-2-(3'-(5-(2-hydroxyethyl)-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

207) 2-((2-(2'-cyano-2-methyl-3'-(4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)pyrrolidine-1-carboxylic acid;

208) ((2-(3'-((2-chloro-5-((5-(difluoromethoxy)pyridin-3-yl)methoxy)-4-(((R)-3-hydroxypyrrolidin-1-yl)methyl)phenoxy)methyl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

209) ((2-(3'-((2-chloro-5-((5-(difluoromethoxy)pyridin-3-yl)methoxy)-4-((3-fluoropyrrolidin-1-yl)methyl)phenoxy)methyl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

210) ((2-(3'-((4-(((2-acetamidoethyl)amino)methyl)-2-chloro-5-((3-cyanobenzyl)oxy)phenoxy)methyl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

211) ((2-(3'-((4-(((S)-2-carboxypyrrolidin-1-yl)methyl)-2-chloro-5-((3-cyanobenzyl)oxy)phenoxy)methyl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

212) ((6-(difluoromethoxy)-2-(3'-(((4,6-dimethoxy-5-(pyrrolidin-1-ylmethyl)pyrimidin-2-yl)oxy)methyl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

213) ((6-(difluoromethoxy)-2-(3'-(((5-((3,3-dimethylazetidin-1-yl)methyl)-4,6-dimethoxypyrimidin-2-yl)oxy)methyl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

214) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-((5-(((((S)-5-oxopyrrolidin-2-yl)methyl)amino)methyl)pyridin-2-yl)oxy)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

215) ((6-(difluoromethoxy)-2-(2'-fluoro-2-methyl-4"-(((((S)-5-oxopyrrolidin-2-yl)methyl)amino)methyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

216) ((6-(difluoromethoxy)-2-(3"-(difluoromethoxy)-2'-fluoro-2-methyl-4"-(((((S)-5-oxopyrrolidin-2-yl)methyl)amino)methyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

217) ((6-(difluoromethoxy)-2-(4"-(((2-hydroxyethyl)amino)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

218) ((6-(difluoromethoxy)-2-(2,2',3"-trimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

219) ((2-(3"-chloro-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline;

220) ((6-(difluoromethoxy)-2-(2"-fluoro-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

221) ((2-(2'-bromo-2"-fluoro-2-methyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline;

222) ((2-(2'-chloro-2"-fluoro-2-methyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline;

223) ((2-(2'-chloro-2"-fluoro-2-methyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

224) ((2-(2'-chloro-2"-fluoro-2-methyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-D-proline;

225) ((6-(difluoromethoxy)-2-(4"-guanidino-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

226) ((6-(difluoromethoxy)-2-(4"-(((3-(dimethylamino)propyl)(methyl)amino)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

227) ((6-(difluoromethoxy)-2-(4"-((3-methoxypyrrolidin-1-yl)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

228) ((6-(difluoromethoxy)-2-(4"-((3-(dimethylamino)pyrrolidin-1-yl)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

229) ((2-(3"-chloro-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

230) ((6-(difluoromethoxy)-2-(2,2',3"-trimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

231) ((2-(2"-chloro-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

232) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-3"-(trifluoromethoxy)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

233) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-3"-(trifluoromethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

234) ((6-(difluoromethoxy)-2-(2,2',3",5"-tetramethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

235) ((6-(difluoromethoxy)-2-(3"-fluoro-5"-methoxy-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

236) ((2-(3"-carboxy-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

237) ((6-(difluoromethoxy)-2-(4"-((3,3-dimethylazetidin-1-yl)methyl)-3"-fluoro-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

238) ((6-(difluoromethoxy)-2-(3"-fluoro-2,2'-dimethyl-4"-((3-methylpyrrolidin-1-yl)methyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

239) ((6-(difluoromethoxy)-2-(3"-fluoro-4"-(((2-hydroxyethyl)amino)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

240) ((2-(3"-cyano-4"-(((S)-3-(hydroxymethyl)pyrrolidin-1-yl)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

241) ((6-(difluoromethoxy)-2-(3"-fluoro-4"-(isoindolin-2-ylmethyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

242) ((6-(difluoromethoxy)-2-(4"-((3-fluoropyrrolidin-1-yl)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

243) ((6-(difluoromethoxy)-2-(3"-fluoro-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

244) ((6-(difluoromethoxy)-2-(3"-(difluoromethoxy)-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

245) ((2-(3"-cyano-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

246) ((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(((S)-3-methylpyrrolidin-1-yl)methyl)pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

247) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(2-((S)-pyrrolidin-2-yl)-1H-imidazol-4-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

248) ((6-(difluoromethoxy)-2-(3"-fluoro-2,2'-dimethyl-4"-(((S)-3-phenylpyrrolidin-1-yl)methyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

249) ((6-(difluoromethoxy)-2-(3"-(4-fluorophenethoxy)-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)proline;

250) ((2-(3"-(cyclopropylmethoxy)-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline;

251) ((2-(4"-(((R)-3-(1H-tetrazol-5-yl)pyrrolidin-1-yl)methyl)-3"-fluoro-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline;

252) ((2-(4"-(((S)-3-((benzyloxy)methyl)pyrrolidin-1-yl)methyl)-3"-fluoro-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)proline;

253) ((6-(difluoromethoxy)-2-(2"-fluoro-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

254) ((6-(difluoromethoxy)-2-(3",5"-dimethoxy-2,2'-dimethyl-4"-(pyrrolidin-1-ylmethyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline hydrochloride;

255) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-4"-(pyrrolidin-2-yl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

256) ((2-(4"-((S)-amino(carboxy)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

257) ((6-(difluoromethoxy)-2-(4"-(((S)-3-((S)-2-((methoxycarbonyl)amino)-3-methylbutanamido)pyrrolidin-1-yl)methyl)-2,2'-dimethyl-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

258) ((6-(difluoromethoxy)-2-(3"-fluoro-2,2'-dimethyl-4"-((5-ureidoisoindolin-2-yl)methyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

259) (S)-1-((2-(3'-(7-cyano-5-(((S)-3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)pyrrolidine-3-carboxylic acid;

260) ((6-(difluoromethoxy)-2-(3"-fluoro-2,2'-dimethyl-4"-((3-ureidopyrrolidin-1-yl)methyl)-[1,1':3',1"-terphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

261) ((2-(3'-(5-(((S)-3-chloropyrrolidin-1-yl)methyl)-7-cyanobenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

262) ((6-(difluoromethoxy)-2-(3'-(4-fluoro-6-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

263) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(6-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

264) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

265) ((6-(difluoromethoxy)-2-(3'-(5-fluoro-6-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

266) ((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(pyrrolidin-1-ylmethyl)pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

267) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(6-oxo-5-(pyrrolidin-1-ylmethyl)-1,6-dihydropyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

268) ((6-(difluoromethoxy)-2-(2'-(difluoromethyl)-3'-(5-fluoro-6-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-2-methyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

269) ((6-(difluoromethoxy)-2-(3'-(5-fluoro-6-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-2'-(fluoromethyl)-2-methyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

270) ((6-(difluoromethoxy)-2-(3'-(2-fluoro-6-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

271) ((6-(difluoromethoxy)-2-(3'-(5-((3,3-dimethylazetidin-1-yl)methyl)-6-methoxypyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

272) ((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(((R)-3-methylpyrrolidin-1-yl)methyl)pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

273) ((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(((S)-3-methylpyrrolidin-1-yl)methyl)pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-D-proline;

274) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)-4-vinylpyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

275) ((6-(difluoromethoxy)-2-(3'-(5-((3-(difluoromethyl)pyrrolidin-1-yl)methyl)-6-methoxypyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

276) ((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-((((5-oxopyrrolidin-2-yl)methyl)amino)methyl)pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

277) ((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(((S)-2-methylpyrrolidin-1-yl)methyl)pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

278) ((2-(3'-(5-(((1s,4s)-7-azabicyclo[2.2.1]heptan-7-yl)methyl)-6-methoxypyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

279) ((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(((R)-2-methylpyrrolidin-1-yl)methyl)pyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

280) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)thiophen-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

281) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(2-(pyrrolidin-1-ylmethyl)pyrimidin-5-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline

282) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(2-(4-methylpiperazin-1-yl)pyrimidin-5-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

283) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(2-(pyrrolidin-1-yl)pyrimidin-5-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

284) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)pyrazin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

285) ((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(pyrrolidin-1-ylmethyl)pyrazin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

286) ((6-(difluoromethoxy)-2-(3'-(6-methoxy-5-(((R)-3-methylpyrrolidin-1-yl)methyl)pyrazin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

287) ((2-(2'-chloro-3'-(6-methoxy-5-((((5-oxopyrrolidin-2-yl)methyl)amino)methyl)pyrazin-2-yl)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

288) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(1,2,3,4-tetrahydroisoquinolin-6-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

289) ((6-(difluoromethoxy)-2-(3'-(isoindolin-5-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

290) ((2-(3'-(2-(2-carboxyethyl)isoindolin-5-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

291) ((2-(3'-(2-(carboxymethyl)isoindolin-5-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

292) ((2-(3'-(2-(1-carboxyethyl)isoindolin-5-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

293) ((2-(3'-(2-amino-1H-benzo[d]imidazol-5-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

294) ((6-(difluoromethoxy)-2-(3'-(5-((3,3-dimethylpyrrolidin-1-yl)methyl)-6-methoxypyridin-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

295) ((2-(3'-(7-cyano-5-(pyrrolidin-1-ylmethyl)-1H-benzo[d]imidazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

296) ((2-(3'-(6,7-difluoro-5-(pyrrolidin-1-ylmethyl)-1H-benzo[d]imidazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

297) ((6-(difluoromethoxy)-2-(3'-(6-fluoro-5-(pyrrolidin-1-ylmethyl)-1H-benzo[d]imidazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

298) ((2-(3'-(6,7-difluoro-1-methyl-5-(pyrrolidin-1-ylmethyl)-1H-benzo[d]imidazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

299) ((2-(3'-(6,7-difluoro-5-(pyrrolidin-1-ylmethyl)-1-(2,2,2-trifluoroethyl)-1H-benzo[d]imidazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

300) ((2-(3'-(4,5-difluoro-6-(pyrrolidin-1-ylmethyl)-1-(2,2,2-trifluoroethyl)-1H-benzo[d]imidazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

301) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-(pyrrolidin-1-ylmethyl)-7-(trifluoromethyl)-1H-benzo[d]imidazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

302) ((2-(2'-chloro-3'-(5-(((2-hydroxyethyl)amino)methyl)picolinamido)-2-methyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline;

303) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine-2-carboxamido)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

304) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(4-methyl-5-(pyrrolidin-1-ylmethyl)oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

305) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(6-(pyrrolidin-1-ylmethyl)-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

306) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(4-(pyrrolidin-1-yl)piperidin-1-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

307) ((6-(difluoromethoxy)-2-(3'-(4-(((1-(hydroxymethyl)cyclopropyl)methyl)amino)piperidin-1-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

308) ((6-(difluoromethoxy)-2-(3'-(4-((3,3-dimethylazetidin-1-yl)methyl)piperidin-1-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

309) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(4-(pyrrolidin-1-ylmethyl)piperidin-1-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

310) ((6-(difluoromethoxy)-2-(3'-(5-((((1R,2S)-2-hydroxycyclopentyl)amino)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-D-proline;

311) ((6-(difluoromethoxy)-2-(3'-(5-((2,2-dimethylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

312) ((6-(difluoromethoxy)-2-(3'-(5-((3,3-dimethylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

313) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-((2-methylazetidin-1-yl)methyl)benzo[d]oxazol-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

314) ((6-(difluoromethoxy)-2-(2,2'-dimethyl-3'-(5-methyl-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridin-2-yl)-[1,1'-biphenyl]-3-yl)benzo[d]oxazol-5-yl)methyl)-L-proline;

315) ((2-(3'-(5-((3-carbamoylpyrrolidin-1-yl)methyl)-7-cyanobenzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline; or

316) ((2-(3'-(7-cyano-5-((3-cyano-3-methylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2-yl)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)-6-(difluoromethoxy)benzo[d]oxazol-5-yl)methyl)-L-proline.

25. A pharmaceutical composition comprising a compound of any one of claims 1-24, or a pharmaceutically acceptable salt or a stereoisomer thereof, and at least one pharmaceutically acceptable carrier or excipient.

26. A method of inhibiting PD-1/PD-L1 interaction, said method comprising administering to a patient a compound of any one of claims 1-24, or a pharmaceutically acceptable salt or a stereoisomer thereof.

27. A method of treating a disease associated with inhibition of PD-1/PD-L1 interaction, said method comprising administering to a patient in need thereof a therapeutically effective amount of a compound of any one of claims 1-24, or a pharmaceutically acceptable salt or a stereoisomer thereof.

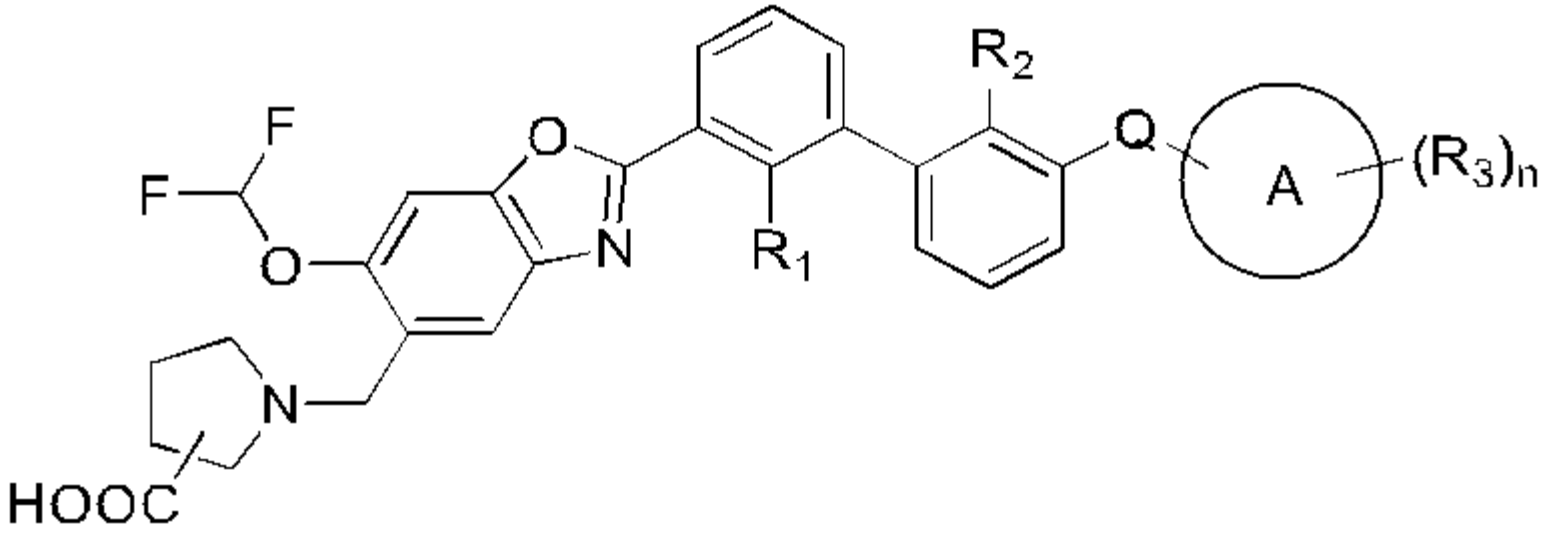
28. The method of claim 27, wherein the disease is colon cancer, gastric cancer, thyroid cancer, lung cancer, leukemia, pancreatic cancer, melanoma, multiple melanoma, brain cancer, renal cancer, prostate cancer, ovarian cancer or breast cancer.

29. A method of enhancing, stimulating and/or increasing the immune response in a patient, said method comprising administering to the patient in need thereof a therapeutically effective amount of a compound of any one of claims 1-24, or a pharmaceutically acceptable salt or a stereoisomer thereof.

30. Use of the pharmaceutical composition of claim 25, or the compound of any one of claims 1-24 for the preparation of a medicament.

31. The use of claim 30, wherein the medicament is used for the treatment or prevention of cancer.

32. The use of claim 30, wherein the cancer is colon cancer, gastric cancer, thyroid cancer, lung cancer, leukemia, pancreatic cancer, melanoma, multiple melanoma, brain cancer, renal



(I)